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DIRECTIONAL AUDIOMETRY

BERTIL NORDLUND
Goteborg Sweden

From the Department of Otolaryngology (Head Prof G Herberts M D) and the Laboratory of Audiology (Head Ass Prof G Lidén M D) Sahlgrenska Hospital, University of Goteborg

Directional hearing was studied in patients with various types of hearing defects in order to estimate the value of directional audiometry as an aid to the topical diagnosis of hearing impairments In a previous paper a method of directional audiometry has been described and analysed In this paper directional hearing was measured by this method in 51 normal hearing subjects and in 101 patients with different types of hearing disorders It was found that patients with conductive losses generally had slightly reduced ability for angular localization Patients with cochlear lesions were found to have a relatively well preserved directional hearing In patients with lesions of the auditory nerve or the pons angular localization was poorer Directional audiometry is considered to be of great value for differentiating between cochlear and so called retrocochlear lesions i e lesions of the auditory nerve or the pons

In a previous paper (Nordlund 1962) a method for the investigation of directional hearing was developed and a literature review of the subject was given The method which is called directional audiometry has two major advantages

(1) It measures what we have called physiological directional hearing , i e the ability to localize a sound source in a free field

(2) It gives individual estimates of the ability to utilize interaural time, phase and intensity differences as clues for directional hearing

Directional hearing tested by this method thus provides a picture of the different functions in angular localization This method of directional audiometry was used in the present study Normal directional hearing according to this method was measured from results obtained in 51 normal hearing persons of different age Directional hearing in patients with various types of hearing loss was investigated and an evaluation of directional audiometry for the diagnosis of hearing defects was made

METHOD

The apparatus for directional audiometry was set up as shown in Fig 1 First the subject was given a brief description of how the test was to be carried out He was then seated in the anechoic chamber with his head one meter from the graduated scale The experimenter sat in the control room from which he could move the loudspeaker at will and read from the directional

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TABLE 1 *The results of the investigation of 101 patients with various hearing defects*

The normal limits are given in Table 2 TM target mark TP, target pattern R and L, thresholds of the right and left ears respectively for the signal in question LP noise low pass filtered white noise MH movable head FH fixed head Case 64 would not continue the directional hearing test as he could not localize the signals at all Abnormal values are given in bold figures

Sex and age	500 cps				2000 cps				4000 cps				LP noise MH		LP noise FH		Av 500 1000, 2000 cps		Speech discr		Rec
	TM	TP	R	L	TM	TP	R	L	TM	TP	R	L	TM	TP	TM	TP	R	L	R	L	
CHRONIC OTITIS																					
♀17	+1	6.3	25	30	−8	11.7	20	20	+13	9.4	30	30	+0	6.0	−2	3.0	23	22	96	96	
♂30	−2	4.4	40	70	−2	8.0	30	45	−2	4.7	20	30	+6	3.3	+5	1.9	33	63	98	90	
34	+4	5.5	75	60	23	17.9	40	20	+4	4.6	25	25	−1	1.9	+2	4.6	58	41	90	94	
♂34	+5	10.3	50	30	−29	23.5	45	20	12	8.5	50	40	−5	4.0	−3	5.1	50	27	79	91	
♂34	+2	4.7	55	35	−21	7.5	35	20	2	6.5	25	25	+1	1.8	+2	3.1	50	33	—	—	
36	−14	8.1	30	60	+13	21.3	40	65	+21	14.7	25	40	+7	6.7	+1	5.2	33	63	92	82	
37	−1	12.8	70	70	−10	13.3	60	35	−1	7.7	60	35	−17	7.5	−5	8.7	62	55	—	—	
46	2	3.2	30	65	−34	28.0	45	55	+13	13.5	25	60	−2	2.3	−1	4.3	35	60	—	—	
14	4	3.5	20	15	−14	25.3	40	−5	−3	7.5	25	5	+0	4.4	+2	1.4	32	7	—	—	
20	−5	4.1	5	25	−3	19.5	10	30	−3	13.3	20	40	−1	1.8	+1	2.7	10	30	—	—	
21	+5	8.6	10	20	+3	15.4	5	25	−4	13.0	15	25	−4	11.0	+13	9.5	6	31	94	98	
29	+9	3.4	20	10	+11	6.4	15	20	+4	8.1	65	65	+8	2.8	+6	2.8	15	8	92	86	
32	−8	8.4	20	40	+12	20.2	10	35	+0	14.5	30	35	−7	4.6	−1	4.0	13	38	—	—	
33	0	2.4	15	30	+8	15.1	25	10	+8	4.8	10	30	+7	3.8	+9	2.0	20	32	96	100	
37	7	5.1	15	45	−4	14.8	5	20	+22	15.6	0	20	−7	4.1	−3	2.8	12	35	—	—	
39	0	5.8	35	70	−12	16.6	25	20	+7	18.6	50	15	−4	2.5	+0	2.4	33	18	—	—	
OTOSCLEROSIS																					
33	3	6	35	80	7	22.9	35	50	−10	12.9	20	30	−1	4.8	+6	3.3	35	68	96	90	
37	+[illegible]	6.6	50	65	+8	24.2	55	60	−2	17.6	50	50	+1	6.0	+3	2.5	55	64	98	100	
37	−2	5.6	50	40	+40	18.1	45	35	−31	16.3	50	20	−5	4.2	−5	4.2	47	38	92	96	
[illegible]4	−0	3.7	45	40	+0	12.5	45	45	−7	5.5	50	55	−2	4.4	−2	4.5	45	41	92	96	
53	15	11.5	50	10	10	15.0	50	15	−11	6.3	70	55	−7	6.2	−5	9.1	50	8	86	90	
53	+1	16.6	65	65	+2[illegible]	13.7	70	70	—	—	—	—	+8	17.3	−11	23.2	67	68	94	94	
58	9	7.3	60	50	−10	15.8	55	45	+2	6.9	45	40	+2	2.2	+0	1.5	57	48	94	96	
59	0	5.4	15	55	10	24.6	35	35	−13	16.9	45	50	+5	3.1	+1	7.2	43	45	98	98	
24	4	5.9	40	30	−3	16.0	30	20	−4	7.2	30	15	−2	2.1	−1	2.6	40	25	100	100	
26	13	10.0	55	50	+0	9.4	55	30	+37	5.8	75	45	+5	3.4	+3	4.7	55	53	94	96	
33	6	14.5	15	40	+[illegible]	11.1	15	25	+1	5.3	10	20	+16	5.8	+5	6.6	15	33	98	100	
37	5	8.5	40	30	37	15.1	25	30	12	10.3	20	40	+11	4.1	+3	4.7	37	27	91	90	
37	6	6.1	50	25	+27	20.2	30	20	53	24.2	40	30	−6	4.2	−5	3.0	40	23	98	96	
45	21	9.8	45	25	−22	15.6	45	40	−22	17.8	45	60	−14	7.8	−13	5.6	42	33	—	—	
46	+10	6.0	30	25	−15	24.5	15	25	+11	13.0	20	40	+4	5.9	+4	3.6	18	23	96	98	
48	−26	24.4	50	40	−14	16.9	40	25	+18	21.6	55	60	−12	6.3	−17	6.8	48	33	98	92	
4[illegible]	+9	4.7	50	25	−36	15.7	40	15	+9	8.1	35	20	+6	4.6	+1	6.2	48	20	96	96	
55	−8	20.8	50	25	+33	19.9	30	10	+1	13.6	40	30	−4	3.8	−7	8.2	40	18	98	94	
55	+62	40.0	15	60	+60	[illegible]	20	40	+56	29.4	35	35	+12	3.1	+7	3.3	15	53	96	96	
56	+15	17.7	60	50	−1	[illegible]	50	95	1	18.0	45	60	−4	4.7	−4	3.7	57	72	98	96	
♀58	−2	7.9	35	60	−15	14.8	45	55	+24	12.7	75	90	−1	4.7	+2	6.4	33	55	88	84	

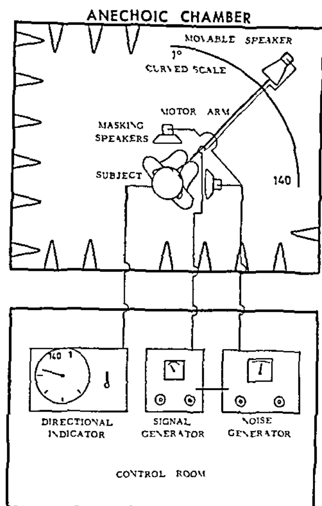


Fig 1 Apparatus used

indicator the position of the loudspeaker relative to the scale The direction of the sound source was judged by the subject, who indicated the corresponding scale mark The difference between the estimated and the true position of the loudspeaker relative to the scale gave the angle of error, and then a measure of the subject's ability to localize a sound source Two types of signals were used pure tones of 500, 2000 and 4000 cps and low pass filtered white noise The intensity was set to a comfortable level for the patient in question, so long as it was sufficiently intense to be discerned by the worse ear In unilaterally deaf patients this condition could, of course, not be met

The patients made 20 judgements of direction at each frequency of 500, 2000 and 4000 cps and 10 determinations for the low pass filtered white noise In making these measurements the patient could turn his head freely from side to side to trace the source of sound

In another series of tests the ability of the patient to localize sounds was measured with the head fixed Otherwise the procedure described above was used but only low pass filtered white noise was used as a signal Between judgements the loudspeaker was moved in steps chosen at random between limits of −30° and +30° on either side of the median plane

TABLE 1 *The results of the investigation of 101 patients with various hearing defects*

The normal limits are given in Table 2 TM target mark TP target pattern R and L, thresholds of the right and left ears respectively for the signal in question, LP noise low pass filtered white noise MH movable head FH fixed head Case 64 would not continue the directional hearing test as he could not localize the signals at all Abnormal values are given in bold figures

Sex and age	500 cps				2000 cps				4000 cps				LP noise MH		LP noise FH		Av 500 1000 2000 cps		Speech discr		Rec
	TM	TP	R	L	TM	TP	R	L	TM	TP	R	L	TM	TP	TM	TP	R	L	R	L	
									CHRONIC OTITIS												
♀17	+ 1	6.3	25	30	− 8	11.7	20	20	+13	9.4	30	30	+ 0	6.0	− 2	3.0	23	22	96	96	
♂30	2	4.4	40	70	− 2	8.0	30	45	− 2	4.7	20	30	+ 6	3.3	+ 5	1.9	33	63	98	90	
♀31	+ 4	5.5	75	60	−23	17.9	40	20	+ 4	4.6	25	25	− 1	1.9	+ 2	4.6	58	41	90	94	
♂34	+ 5	10.3	50	30	29	23.5	45	20	−12	8.5	50	40	− 5	4.0	− 3	5.1	50	27	79	91	
♂34	2	4.7	55	35	21	7.5	35	20	− 2	6.5	25	25	+ 1	1.8	+ 2	3.1	50	33	—	—	
♂36	14	8.1	30	60	+13	21.3	40	65	+21	14.7	25	70	+ 7	6.7	+ 1	5.[illegible]	33	63	92	82	
♀37	1	12.3	70	70	10	13.3	60	35	− 1	7.7	60	35	−17	7.[illegible]	− 5	8.7	62	55	—	—	
♂46	2	3.2	30	65	34	28.0	45	55	+13	13.5	25	60	− 2	2.3	− 1	4.3	35	60	—	—	
♂14	4	3.5	20	15	14	[illegible]	40	−5	− 3	7.5	25	5	+ 0	4.4	+ 2	1.4	32	7	—	—	
♂20	5	4.1	5	25	3	19.5	10	30	− 3	13.3	20	40	− 1	1.8	+ 1	2.7	10	30	—	—	
♂21	+ 5	8.6	10	20	+ 3	15.4	5	25	4	13.0	15	25	− 4	14.0	+13	9.5	6	31	94	98	
♂29	+ 9	3.4	20	10	+11	6.4	15	20	+ 4	8.1	65	65	+ 8	2.8	+ 6	2.8	15	8	92	86	
♂3[illegible]	8	8.4	20	40	+12	20.[illegible]	10	35	+ 0	14.5	30	35	− 7	4.6	1	4.0	13	38	—	—	
♂33	0	2.4	15	30	+ 8	15.1	25	40	+ 8	4.8	10	30	+ 7	3.8	+ 9	2.0	20	32	96	100	
3[illegible]	[illegible]	5.1	15	45	− 4	14.8	5	20	+2[illegible]	15.6	0	20	− 7	4.4	3	2.8	12	35	—	—	
39	0	5.8	35	20	−12	16.6	75	20	+ 7	19.6	50	15	− 4	2.5	+ 0	2.4	33	18	—	—	
									OTOSCLEROSIS												
♀31	3	6.7	35	80	7	22.9	35	50	10	12.9	20	30	1	4.8	+ 6	3.3	35	68	96	90	
3	+ 8	6.6	50	65	+ 8	21.[illegible]	55	60	− 2	17.6	50	50	+ 1	6.0	+ 3	2.5	55	64	98	100	
♀3	2	5.6	50	40	+40	18.1	45	35	−31	16.3	50	20	− 5	4.2	− 5	4.2	4	38	92	96	
47	+ 0	3.7	45	40	+ 0	12.5	45	45	− 7	5.5	50	55	2	4.4	2	4.5	45	41	92	96	
♂53	15	11.5	50	10	−19	15.0	50	15	−14	6.3	70	55	− 7	6.2	− 5	9.1	50	8	86	90	
53	+ 1	16.6	65	65	+[illegible]	13.7	70	0	—	—	—	—	+ 8	17.3	−11	23.2	67	68	94	94	
♀58	9	7.3	60	50	10	15.8	55	45	+ [illegible]	6.9	45	40	+ 2	2.2	+ 0	1.5	57	48	94	96	
♀59	0	5.4	45	55	10	24.5	35	35	13	16.9	45	50	+ 5	3.1	+ 1	7.[illegible]	43	45	98	98	
♀21	4	5.9	40	30	− 3	16.9	30	20	4	7.2	30	15	− 2	2.1	− 1	2.6	40	25	100	100	
♂21	13	10.0	55	50	+ 0	9.4	55	30	+37	5.8	75	45	+ 5	3.4	+ 3	4.7	55	53	94	96	
♀33	6	14.[illegible]	15	40	+ 2	11.1	15	25	+ 1	5.3	10	20	+16	5.8	+ 5	6.6	15	33	98	100	
♀37	5	8.5	40	30	−37	15.1	25	30	−12	10.3	20	40	+11	4.1	+ 3	4.7	37	27	94	90	
♀3	6	6.1	50	25	+27	20.2	30	20	−53	24.2	40	30	− 6	4.2	5	3.0	40	23	98	96	
♀45	[illegible]1	9.8	45	25	−22	15.6	45	40	−22	17.8	45	60	−14	7.8	−13	5.6	4[illegible]	33	—	—	
♀46	+10	6.0	30	75	−15	24.1	15	25	+11	13.0	20	40	+ 4	5.9	+ 4	3.6	18	23	96	98	
♂48	26	[illegible]	50	40	−14	16.2	40	25	+19	21.6	55	60	−12	6.3	−17	6.3	48	33	98	92	
♂49	+ 9	4.7	50	25	36	15.7	40	15	+ 9	8.1	35	20	+ 6	4.6	+ 4	6.2	48	29	96	96	
♀55	8	[illegible]0.8	50	25	+33	19.0	30	10	+ 1	13.6	40	30	− 1	3.8	7	8.2	40	18	98	94	
♀55	+6[illegible]	40.0	15	60	+60	[illegible]	20	40	+56	[illegible]9.4	35	35	+12	3.1	+ 7	3.3	15	53	96	96	
♂56	+15	17.[illegible]	60	50	− 1	29.5	50	95	− 1	18.2	45	60	− 4	4.7	− 4	3.7	53	72	98	96	
♀58	2	7.9	35	60	15	14.8	45	55	+24	12.7	75	90	− 1	4.7	+ 2	6.4	33	55	88	84	

Tab 1 (continued)

No	Sex and age	500 cps TM	500 cps TP	500 cps R	500 cps L	2000 cps TM	2000 cps TP	2000 cps R	2000 cps L	4000 cps TM	4000 cps TP	4000 cps R	4000 cps L	LP noise MH TM	LP noise MH TP	LP noise FH TM	LP noise FH TP	AA 500, 1000, 2000 cps R	AA 500, 1000, 2000 cps L	Speech discr R	Speech discr L
										COCHLEAR LESIONS											
38	♀12	+ 4	8.7	5	5	−14	12.7	25	30	− 6	7.0	25	30	+ 1	1.5	+ 2	1.8	20	14	60	70
39	♂12	− 1	10.4	45	45	+ 6	14.4	50	50	− 1	2.6	50	50	− 1	2.5	+ 0	3.3	48	46	86	88
40	♀12	+ 1	5.5	20	20	− 6	10.2	35	35	− 3	7.7	5	15	− 1	2.2	− 1	2.0	30	27	88	94
41	♀19	− 6	6.7	55	60	− 8	10.5	50	55	− 3	9.9	20	10	− 1	2.9	− 1	3.1	55	57	76	84
42	♀23	− 6	11.0	70	70	−11	12.7	60	60	− 2	10.2	60	55	+ 8	4.3	+ 4	5.6	67	65	12	18
43	♂30	+ 2	4.9	15	30	+ 3	12.3	30	35	+ 0	5.3	30	45	+ 2	2.2	+ 2	3.0	22	32	82	74
44	♀33	− 1	3.1	30	30	+ 3	13.1	55	50	+ 2	8.0	65	60	+ 1	1.5	+ 0	1.4	42	40	72	86
45	♀37	− 3	3.0	65	50	− 3	12.9	35	35	+ 1	9.4	30	20	− 2	1.8	+ 1	4.7	17	42	92	90
46	♀37	+ 3	5.3	40	40	−20	12.8	40	50	− 9	12.0	40	45	+ 2	2.5	+ 1	2.9	33	40	96	94
47	♂40	+ 5	3.0	0	5	+ 0	13.2	30	55	+ 5	7.1	30	45	+ 0	2.2	+ 0	1.7	12	23	92	86
48	♀48	+ 8	10.7	60	55	−17	9.8	55	50	− 5	6.6	45	50	+ 0	4.7	+ 1	3.2	58	53	18	28
49	♀51	− 4	3.3	40	40	−21	11.6	20	15	+ 1	7.5	0	0	+ 0	2.3	+ 0	1.0	33	31	98	100
50	♂56	− 9	9.9	35	50	−21	9.4	50	55	−15	8.8	65	55	− 5	2.6	− 1	3.4	45	53	58	78
51	♀13	− 1	5.0	30	15	− 5	12.5	30	10	+ 0	11.3	30	5	+ 1	3.1	+ 0	2.9	32	15	74	98
52	♂29	− 8	5.1	50	10	− 5	4.1	40	0	− 3	4.3	50	10	− 6	2.5	−10	3.6	45	7	92	100
53	♂33	+17	6.4	10	25	− 8	6.3	0	35	+ 9	4.5	15	60	+ 5	2.1	+ 1	3.1	5	30	96	90
54	♂34	− 6	4.8	40	5	+21	21.5	45	10	+ 5	3.7	50	0	+ 3	3.3	− 1	6.3	43	10	48	94
55	♀38	− 4	5.5	20	10	+ 4	9.4	35	10	+21	14.4	40	0	− 4	4.5	− 3	2.2	28	8	88	100
56	♂44	− 6	3.2	35	5	− 5	13.4	35	5	−27	15.0	65	40	− 5	3.5	− 8	7.1	50	6	92	88
57	♂52	− 4	3.5	5	10	− 9	8.2	10	15	− 3	6.8	25	35	+ 2	2.0	+ 2	2.0	8	10	90	90
58	♀59	− 6	11.2	10	45	+ 2	18.5	5	50	+ 5	15.7	25	45	− 6	5.3	− 1	5.5	10	50	90	62
59	♂69	+ 1	4.4	5	25	−35	17.9	15	60	− 6	12.8	60	65	+ 4	1.0	+ 2	2.3	10	10	92	60
										LESIONS OF THE AUD. NERVE OR THE PONS REGION											
60	♀36	−15	33.2	0	10	+ 6	17.1	5	40	− 5	6.0	5	45	+13	2.6	+ 9	3.2	2	25	90	88
61	♂40	+ 8	13.2	−5	10	+ 0	18.7	−5	5	+30	16.0	−5	65	+29	10.0	+22	10.5	2	8	92	74
62	♀42	− 9	21.8	25	15	+31	46.2	20	25	+12	14.3	25	20	+12	27.5	+ 4	19.0	22	18	0	[illegible]
63	♂50	+ 7	27.8	5	10	+13	25.5	10	20	+10	35.9	15	60	+33	18.6	+ 1	33.3	10	17	—	—
64	♂50	—	—	55	−5	—	—	50	5	—	—	70	25	—	—	—	—	53	0	0	98
65	♀56	−24	5.7	30	15	−29	13.7	40	15	−33	9.6	70	10	−31	6.8	−19	11.9	37	14	82	96
66	♀56	+ 1	7.8	45	35	−10	11.5	35	35	− 3	8.8	70	50	+ 3	6.0	− 1	8.1	40	33	96	86
67	♀64	+19	17.7	10	20	−13	9.2	0	5	−15	7.1	25	20	6	6.9	−11	6.8	7	10	74	90
										BRAIN LESIONS											
68	♂47	− 1	3.2	20	0	−15	13.4	10	10	− 5	12.0	25	15	− 1	1.1	+ 0	2.0	17	7	96	54
69	♂48	− 2	5.5	−5	0	−14	16.6	0	0	+ 5	6.8	0	0	+ 0	4.6	+ 2	5.2	3	0	—	—
70	♂48	+ 1	4.9	10	10	+ 8	23.5	20	25	− 7	12.0	30	30	+ 3	2.0	+ 2	2.0	15	17	98	94
71	♀49	− 9	8.1	5	20	+ 0	18.1	20	10	−14	8.0	15	10	+ 0	1.7	+ 2	3.0	12	15	94	94
72	♀56	− 8	7.3	25	20	− 4	15.0	10	5	− 5	6.5	10	10	− 1	2.4	− 2	1.9	18	15	–	—
73	♂61	+ 1	7.5	5	0	−16	8.2	15	5	+ 0	6.4	35	10	+ 1	2.2	+ 1	3.9	13	5	100	100
74	♂62	+ 8	7.2	35	60	− 8	11.7	60	60	+ 9	6.5	50	45	+12	5.0	+10	3.9	43	60	94	78
75	♀64	+ 8	5.7	10	20	− 4	5.9	20	25	− 1	7.7	70	40	+ 3	2.8	+ 1	3.7	17	22	92	94
76	♂65	− 1	3.3	25	20	−11	38.2	50	65	− 6	9.5	60	70	+ 6	1.5	+ 5	3.4	35	35	—	—

1 (continued)

Sex and age	500 cps				2000 cps				4000 cps				LP noise MH		LP noise FH		Av 500, 1000, 2000 cps		Speech discr		
	TM	TP	R	L	TM	TP	R	L	TM	TP	R	L	TM	TP	TM	TP	R	L	R	L	Rec
Combined lesions																					
♂ 37	+ 2	3 8	40	40	− 1	17 3	40	45	− 4	8 6	25	30	+ 0	2 5	− 2	5 1	12	43	96	96	−
♀ 43	+ 3	5 2	15	60	− 10	10 8	15	45	− 11	6 1	15	45	− 2	4 2	+ 0	3 1	15	48	100	74	−
♂ 50	+ 2	5 2	10	15	− 27	22 7	45	10	+ 0	6 6	50	40	− 4	2 0	− 1	2 2	25	18	80	90	
♂ 51	− 3	6 8	5	5	+ 8	8 2	45	45	+ 6	9 1	50	50	+ 2	2 3	+ 0	3 0	22	22	—	—	+
♂ 52	+ 0	9 1	25	10	− 31	16 7	60	70	− 19	7.2	85	75	+ 1	4 7	+ 4	5 3	42	38	86	64	
♀ 53	− 6	12 5	15	15	− 15	16 0	35	40	− 1	10 7	40	30	− 8	2 2	− 4	2 0	28	28	88	90	
♂ 57	− 3	2 6	5	0	− 27	19 2	15	15	− 2	6 2	60	65	+ 3	2.8	+ 5	2 0	10	10	80	70	
♂ 73	+ 8	23.5	10	15	+ 9	13 0	30	15	+ 4	9 1	60	50	+ 7	3 4	+ 9	5 9	18	15	94	88	
♂ 74	− 6	7 0	40	40	− 48	29 0	75	30	− 57	30 6	95	35	− 12	3 7	− 9	5 5	55	35	86	88	
♀ 76	− 3	7 2	40	15	− 16	12 6	55	60	− 12	7 0	65	65	+ 2	4 1	− 10	6.5	49	52	60	42	
Unilat deaf																					
♀ 9	+ 0	46.5	5	—	− 21	37 0	0	—	− 34	54 1	5	—	− 13	51 0	+ 4	20 8	2	—	—	—	
21	10	15.1	—	30	− 13	26.0	75	20	—	—	5	35	− 7	5 1	− 5	4 9	—	2?	—	—	
21	8	28.5	—	30	+ 25	25.6	—	0	+ 1	33.3	—	15	+ 20	12 2	− 16	19 3	—	15	—	96	
24	+ 19	25 7	0	—	+ 19	29 9	5	—	+ 44	29 7	5	—	+ 30	18.6	+ 53	19 1	2	—	—	—	
34	+ 33	27 6	0	—	+ 19	21 7	15	—	+ 31	21 2	25	—	+ 48	36.8	+ 36	18.7	8	—	—	—	
36	+ 1	14 4	—	5	− 10	55.9	−	0	− 21	27.1	—	5	+ 3	10 9	− 41	26.4	—	3	—	—	
37	+ 9	9 3	75	20	− 14	19 4	90	40	− 10	9 9	—	65	5	7 5	+ 0	14 2	85	30	16	88	
42	+ 6	14 9	—	20	− 12	29 9	—	10	− 2	18.2	—	20	+ 0	19 2	− 3	25.9	—	12	—	—	
42	+ 15	22 9	20	—	+ 16	40 6	10	—	+ 24	21 0	15	—	4	16.3	+ 3	23.0	13	—	—	—	
47	5	21 2	—	20	− 7	19 9	—	35	+ 1	6 5	—	45	+ 7	20 0	− 3	17 5	—	22	—	—	
Lesions of the vest nerve																					
34	+ 0	4 4	0	5	− 6	14 7	10	5	+ 3	7 1	5	10	+ 2	0 5	+ 0	2 6	3	2	—	—	
38	+ 0	3 9	5	10	− 12	19 2	10	10	− 11	14 4	10	10	+ 5	2 4	+ 4	2.6	10	10	—	—	
38	2	7 7	15	15	+ 6	6 1	15	20	− 2	6 2	15	30	+ 2	3 1	+ 3	2 2	13	17	94	96	
47	+ 0	2 2	15	15	− 14	17 8	15	10	− 9	9 7	30	25	+ 2	1 3	+ 2	2 4	15	12	86	96	
63	+ 1	4 9	5	0	14	14 0	15	10	− 1	8 0	25	30	+ 3	3 6	+ 4	1 9	6	5	92	90	

The average position relative to the actual position of the loudspeaker given by the subject was called 'target mark', and the standard deviation was called the 'target pattern'.

MATERIAL

The 51 normal hearing subjects tested represented four different age groups. 21 were between 15 and 30 years of age and 10 in each of the groups between 31–45 years, 46–59 years, and over 59 years. All had normal eardrums and their pure tone audiograms could be regarded as normal for their age groups. Some of the subjects had noise induced losses at the frequencies 2000 and 4000 cps, and their results for these signals were therefore excluded. Their hearing was fairly symmetrical. The average target

marks and target patterns of the different age groups for each type of signal were subjected to an analysis of variance

Patients with various types of hearing defects have also been tested in the same way. This group consisted of 101 patients with the following types of lesions, as shown in Table 1: Middle ear lesions (Nos 1–37), cochlear lesions (Nos 38–59), lesions of the auditory nerve or the pontile region (Nos 60–67), other lesions of the central nervous system (Nos 68–76), combined lesions, i e. cochlear and suspected lesions of the central nervous system (Nos 77–86), *unilaterally deaf (Nos 87–96) and lesions of the vestibular nerve (Nos. 97–101)* The patients were examined with pure-tone audiograms and in most cases with speech audiogram The presence of recruitment was judged from the stapedius reflex test and indirectly from the Békésy audiogram

The patients with middle ear lesions presented no diagnostic difficulties The diagnoses in this group were in 16 cases chronic otitis media (Table 1, Nos 1–16) in eight cases otosclerosis (Nos 17–24) Eight patients had previously had stapes surgery (Nos 25, 27, 28, 31, 33, 35, 36 and 37) and five had had the fenestration operation (Nos 26, 29, 30, 32 and 34)

The patients with cochlear lesions (Nos 38–59) presented in most of the cases no diagnostic difficulties The presence of recruitment or known etiology (for instance, noise-induced loss) indicated that the lesions were located in the cochlea The diagnoses in this group were sensorineural loss of cochlear type, in 13 cases bilateral (Nos 38–50) and in nine cases unilateral (Nos 51–59) There were various causes, including hereditary cochlear degeneration, labyrinthine hydrops, Mb Ménière, and acoustic trauma

The patients with lesions of the auditory nerve or the pons (Nos 60 67) presented *in most of the cases no diagnostic difficulties This group is demonstrated in Table 3* Case No 63 deserves special mention This patient was suffering from a unilateral left-sided sudden deafness While the hearing in the affected ear improved, the Békésy audiogram and recordings of the stapedius reflex showed no recruitment present The above mentioned facts support the diagnosis of a left sided acoustical neuritis The pure-tone audiogram eventually became almost normal, only a dip at 1000 cps remaining This was the condition when the patient was investigated with directional audiometry

The patients with brain lesions had in all cases been examined in the department of neurology All of the diagnoses were considered quite certain Four cases had different kinds of brain tumors, two had tumors of the pituitary gland, one had cerebral atrophy, one had had a cerebrovascular accident and one case had disseminated sclerosis

The patients with "combined lesions", i e cochlear lesions with suspected central lesions, constitute a more heterogeneous group, and the diagnoses were not certain

The unilaterally deaf patients presented no diagnostic difficulties They had normal hearing in one ear and the other ear was deaf Two of the patients, however, had some hearing in the "deaf" ear and two patients had mild sensorineural losses in the healthy ear

The patients with lesions of the vestibular nerve presented no diagnostic difficulties. They had normal hearing but a strongly impaired vestibular function on one or both sides. The vestibular function was investigated with caloric tests.

The target marks and target patterns have been calculated for all patients and for each type of signal (Table 1).

STATISTICS

The normal limits for the target marks and the target patterns were calculated as follows. First, analyses of variance were undertaken to find out whether the observations were correlated with age. No significant differences were found, however, between the different age groups. Consequently all the observations were treated as one group.

Each individual was characterized by

(1) target mark = the mean of 20 differences between the true position of the loudspeaker and its position as judged by the subject. (When low pass filtered white noise was used as a signal only 10 determinations were made, because the spread of the observations was so small.)

(2) target pattern = the standard deviation of the above mentioned differences. As the number of observations for each individual is fairly large, it is permissible to assume that both target marks and target patterns are normally distributed. After means and standard deviations had been estimated 99.9% normal intervals were calculated, two sided for the target marks and one sided for the target patterns. The intervals are given in Table 2.

TABLE 2. *Normal limits of the target marks and the target patterns*

				Noise	
	500 cps	2000 cps	4000 cps	*MH*	*FH*
Target marks	−10 − +8 (−10.1 + 7.7)	−30 − +20 (−30.3 + 20.1)	−14 − +12 (−14.4 + 11.4)	−6 − +8 (−6.0 + 7.0)	−6 − +8 (−6.7 + 7.3)
Target patterns	12 (11.4)	24 (23.9)	16 (16.2)	6.0 (5.4)	6.0 (5.2)

RESULTS

Th[illegible]

onl[illegible]

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Normal hearing

The results in the 51 normal hearing subjects are shown in Fig. 2. Note particularly the different magnitude of the target patterns, i.e. standard deviations with different signals. This clearly demonstrates the differences in

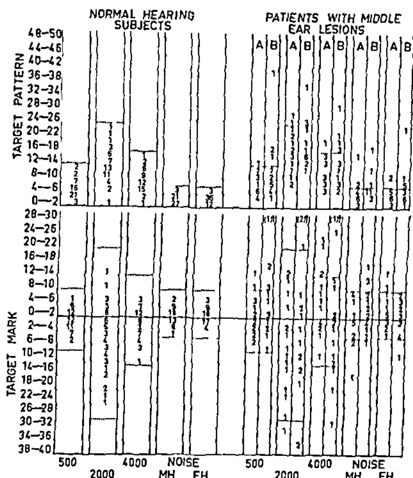


Fig. 2. The distributions of the target marks and the target patterns of the normal hearing subjects and the patients with middle ear lesions. Patients with chronic otitis (Nos. 1–16) were plotted in the A columns. Patients with otosclerosis (operated and not operated Nos. 17–37) were plotted in the B columns. Five fenestrated patients are excluded. The unit is in degrees. A negative target mark (— = below 0) corresponds to a localization error to the left side of the true position of the loudspeaker and vice versa. MH movable head. FH fixed head. Dotted lines represent the normal limits.

accuracy of localization with different types of sound. The largest pattern is found with 2000 cps and the least with low pass filtered white noise. The normal limits for the target patterns and target marks are also shown in the Figs. 2–5 and as can be seen (Fig. 2) all values for the normal subjects lie within these limits. A patient whose target mark or target pattern exceeds these limits for one or more of the different types of signals is considered to have abnormal directional hearing. The possibility that directional hearing may be correlated with hearing acuity was investigated by plotting target patterns and target marks against pure tone thresholds, threshold differences between the two ears and various combinations of these values for all normal patients. These scatter plots, however, revealed no correlation.

The results of the investigations of the patients with hearing defects are given in Tables 1 and 3. Figs. 2–5 demonstrate the distributions of the target marks and target patterns in the diff

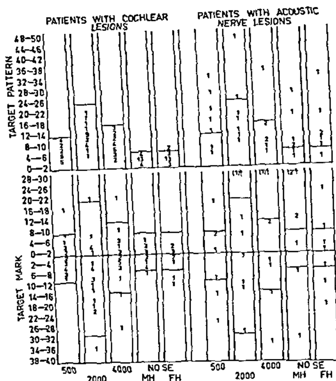


Fig 3 The distributions of the target marks and the target patterns of the patients with cochlear lesions (Nos 38 59) and the patients with lesions of the auditory nerve (Nos 60–67) The last group included two patients with disseminated sclerosis with suspected lesions of the pons region (Nos 66 and 61)

Middle ear lesions

Some of the patients with middle ear lesions had abnormal directional hearing as judged by both target patterns and target marks (Table 1 and Fig 2) The patients with chronic otitis (Nos 1–16) showed abnormal directional hearing in 10 out of the 16 cases The patients with *non operated oto sclerosis* (Nos 17 24) showed abnormal directional hearing in five out of the eight cases The fenestrated patients (Nos 26 29 30 32 and 34) all have abnormal directional hearing Case No 26 has symmetrical hearing loss due to a non functioning fenestra The directional audiogram shows two abnormal target marks but normal target patterns The other four cases have at least two abnormal target marks together with one abnormal target pattern Case No 30 is a bilaterally fenestrated patient with functioning fenestrae and relatively symmetrical hearing Directional hearing however, *is clearly* abnormal Among the stapes mobilized patients only one (No 25) showed normal directional hearing This patient had only a moderate hearing loss for pure tones The other three patients had abnormal directional audiograms and more severe hearing loss for tones All four of the stapedectomized patients (Nos 27 28 31 and 37) showed abnormal directional audiograms,

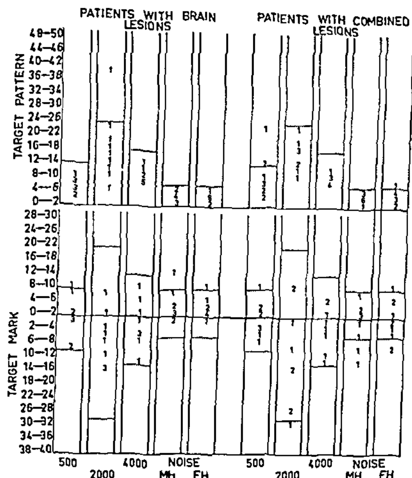


FIG 4 The distributions of the target marks and the target patterns of the patients with brain lesions (Nos 68 76) and the patients with combined' lesions, i e cochlear lesions with suspected central lesions (Nos 77–86)

although the operation had been successful in three of them and the pure tone audiograms were almost normal Thus again no correlation was found between directional and pure-tone audiograms

Cochlear lesions

The patients with *cochlear lesions* had a relatively good directional hearing This was especially true as judged by the target patterns Only two patients *(Nos 54 and 56) had one abnormal target pattern each which was recorded* with low pass filtered white noise and fixed head, and these target patterns just exceeded the normal limits When the target patterns for all cases with cochlear lesions are compared with the target patterns of the normal hearing subjects (Figs 2–3) it is noted with the 500 cps *signal that values for most of* the normal subjects lie between 2–4 degrees while the patients with cochlear lesions center around 4 6 degrees The same situation is noted at 2000 and *4000 cps and with low pass filtered white noise with movable head On the* other hand, with low pass filtered white noise and fixed head both groups center around 2–4 degrees Thus it is interesting to note that although some

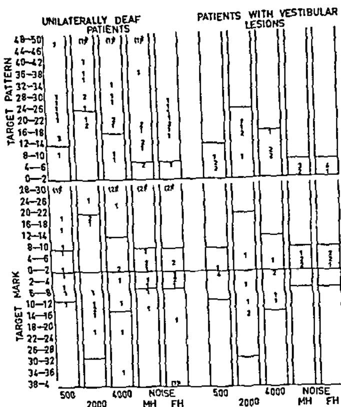


FIG 5 The distributions of the target marks and the target patterns of the unilaterally deaf patients (Nos 87 96) and patients with vestibular lesions (Nos 97 101)

of the cases with cochlear lesions had abnormal target marks, they still had normal target patterns

Auditory nerve lesions

All of the patients with lesions of the auditory nerve or the pons had one or more abnormal target patterns and most of them one or more abnormal target marks (Tables 1 and 3, and Fig 3) There is thus a marked difference between this group and the group of patients with cochlear lesions

Other lesions

The patients with brain lesions generally had normal directional hearing (Table 1 and Fig 4) The patients who in addition to cochlear defects had suspected central lesions had in some cases abnormal target patterns and target marks

All of the unilaterally deaf patients had abnormal target patterns and in most cases abnormal target marks

All of the patients with vestibular dysfunction but with normal hearing had also normal directional hearing

DISCUSSION

Greene (1929) made a clinical investigation of the ability to localize sounds in patients with tumors of the brain. He determined the ability of the patients (1) to localize a buzzing sound source (2) to discriminate interaural time and intensity differences presented through a stethoscope. He investigated a normal group and 51 cases of neurology lesions. He found abnormal directional hearing in 18 of the pathological cases. *The group with abnormal directional* hearing included a higher percentage of tumors of the temporal lobe than the group with normal directional hearing. He stated as probable conclusions that lesions of the temporal lobe and increased intracranial pressure can impair directional hearing.

Jongkees *et al.* (1957) examined directional hearing in a group of patients suffering from various types of hearing loss. He investigated the ability to localize a 1000 cps tone in the horizontal plane in a free field with the head fixed. He found in normal hearing persons an S shaped diagram when the objective position was plotted along the abscissa and the subjective position *is plotted along the ordinate. The pathologic groups consisted of chronic* otitis media, atresia, nerve deafness, otosclerosis, fenestration, tympanoplasty and unilateral total deafness. He concluded: "It was evident from these examinations that neither a conduction deafness nor a difference in hearing acuity of the two ears necessarily resulted in an impairment of directional hearing. Patients from the perception deafness group often had impaired directional hearing. However, no relationship between the types of audiograms either in air conduction or in bone conduction and the degree of loss in directional hearing could be found. Otosclerosis patients (subjected to fenestration or not) all showed strongly disturbed directional hearing. The hy*pothesis is submitted that in these patients a change in time and phase pat*tern may cause the loss of directional hearing. Unilateral total deafness does not necessarily prevent directional hearing. In our series of 10 patients two had normal directional hearing and one a slight impairment only."

Matzker & Welker (1959) described a method of directional hearing as an aid in the topical diagnosis of brain lesions. The patient listens to an intermittent sinusoidal tone through earphones. When the stimulus from one earphone is delayed in time the sound source seems *to move towards the* other ear. Matzker has used different frequencies but has not been able to eliminate clicks in the apparatus. This means that it is probably always the same thing that is investigated in the Matzker test, i.e. the ability to discriminate interaural time differences. He concluded that directional hearing tested in this way was found to be increasingly less accurate with advancing years. Patients with tumors of the brain were investigated and he found abnormal directional hearing in these patients (six cases are *reported). He therefore* concluded that the test is of great value in detecting brain lesions. The method is inapplicable in the presence of conductive or perceptive deafness.

There are thus diverging opinions as to the value of directional hearing

in the topical diagnoses of hearing defects The methods have been incomplete and it is difficult to get the patients to locate a phantom source in the head as produced by binaural stimulation through ear phones The method used in the present study is physiological in that the sound source is located where it actually is It is thus simple to understand and to perform

The ability to localize 500 cps is based on the interaural phase difference the 2000 and 4000 cps tones on the interaural intensity difference and low pass filtered white noise mainly on the interaural time difference It is thus possible by using the different signals to differentiate between the ability to utilize interaural time phase and intensity differences as clues to directional hearing The ability to utilize interaural time differences is also judged with a fixed head The observations are analysed in two ways (1) the mean of the differences between the true position of the loudspeaker and the position as judged by the subject i e target mark and (2) the standard deviation of these differences i e target pattern In this way we get a picture of the different functions involved in directional hearing and especially the target pattern is a criterion of the interaction between the two ears

The results in the normal hearing subjects showed different magnitudes of the target patterns with different kinds of signals depending upon the various above mentioned physiological and physical limitations for localizing the different signals They did not show any significant differences in target patterns and target marks in the different age groups It is possible this might have been the case if the number of subjects had been larger The difference however if existing is small and thus the normal limits are independent of age which is very convenient from a clinical point of view In Fig 2 we can see that the target marks of the normal subjects for the signals 500 2000 and 4000 cps have a tendency towards the negative side From the results of the physical measurements of the sources of error of this method this condition could be predicted for the 500 and 2000 cps signals (Nordlund 1962) At 4000 cps it was not so clear but there is probably a physical reason at this frequency also The target marks of low pass filtered white noise have a tendency towards the positive side The physical prerequisites for localizing this signal could not be measured It is reasonable to suggest however that this tendency may also have a physical cause

An analysis of the observations with fixed head showed about the *same* tendency to give an S shaped curve as Jongkees has described The directional hearing was also significantly better within the range +15°– –15° from the median plane than within +15°– +30° and –15°– –30°

The investigations of the patients with middle ear lesions showed an impaired directional hearing especially in the otosclerosis group There is thus a decreased ability to discriminate the interaural differences of time phase and intensity in these cases These findings confirm the findings of Jongkees

The relatively well preserved directional hearing in patients with cochlear lesions and especially the normal target patterns is remarkable It is evident that cochlear lesions have only a slight influence on a patient s ability to

DISCUSSION

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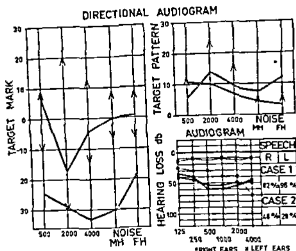


Fig 6 Directional audiogram Case 1 (dotted curves) was a patient with a right sided acoustic neurinoma Note the mild sensorineural loss in the pure tone audiogram and the almost normal speech discrimination score The abnormal target marks at the signals 500 4000 and noise (MH and FH) and the abnormal target patterns at the noise (MH and FH) indicate a probable lesion of the auditory nerve (No 65) The arrows represent the normal limits of the target marks and target patterns Case 2 (solid lines) had bilateral cochlear lesions (No 48) Note the pathological speech discrimination score and tone audiogram but normal target marks and target patterns for all the signals MH movable head FH fixed head

discriminate the interaural differences of time phase and intensity A unilateral or bilateral impairment of speech discrimination with raised threshold for pure tones is not always accompanied by an impaired directional hearing From a practical clinical point of view this distinction is very important as all the patients with lesions of the auditory nerve or the pontile region had abnormal directional hearing The great difference regarding directional hearing between the patients with cochlear lesions and patients with lesions of the auditory nerve or the pons can be studied in Fig 3 It is especially the target patterns which in the last group exceed the normal limits This group is also demonstrated in Table 3 where other diagnostic signs are also presented Patients 65 60 62 and 67 have surgically verified lesions The diagnoses in Patients 64 and 63 can also be considered quite certain The site of the lesion in Patients 66 and 61 on the other hand are not certain It is probable however that lesions of the pons are present in these cases X ray examinations of the internal meatus were pathological in case 60 The caloric examinations showed abnormal values in cases 65 60 62 and 67 A tone decay test to study the adaptation was carried out in cases 60 62 and 64 but was abnormal only in case 64 The discrepancy between the pure tone audiogram and the speech discrimination scores in cases 62 and 64 made a retrocochlear lesion suspect The target marks were clearly pathological in all cases in this group except case 66 The target patterns were abnormal in all the cases in this group This is of great value when considered in relation to some of the other investigated persons i e the 51 normal hearing persons

TABLE 3 *Patients with lesions of the auditory nerve or the pons*

Case No	Diagnosis	Therapy	X Ray port acust int	Caloric examination	Decay	Type of loss in tone audiogram	Speech discrim R (%)	Speech discrim L (%)	IM	TP
65	Acust neurinoma *dx*	Operation	Uncertain	Abnormal	—	Mild sensori neural loss on right side	82	96	Abnormal	Abnormal
60	Acust neurinoma sin	Operation	Abnormal	Abnormal	Normal	Mild sensori neural loss on left side	90	88	Abnormal	Abnormal
62	Acust neurinoma *dx*	Operation	Normal	Abnormal	Normal	Normal	0	Normal	Abnormal	Abnormal
	…g reg angul sin	Operation	Normal	Abnormal	—	Normal	71	90	Abnormal	Abnormal
	…l encephalopathia sin V, VII VIII	Medical treatment	Normal	Normal	Abnormal	About 60 db sensorineural loss on right side	0	98	Abnormal	Abnormal
	…t neuritis sin	Medical treatment	—	—	—	Sensorineural dip at 4000 cps on left side	—	—	Abnormal	Abnormal
	…osis diss	Medical treatment	Normal	—	—	Bilateral mild sensorineural loss	96	86	Normal	Abnormal
	…osis diss	Medical treatment	Normal	Uncertain	—	Sensorineural dip at 4000 cps on left side	92	71	Abnormal	Abnormal

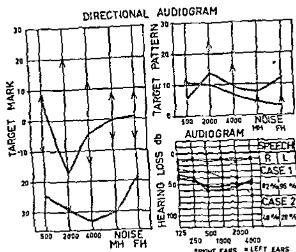


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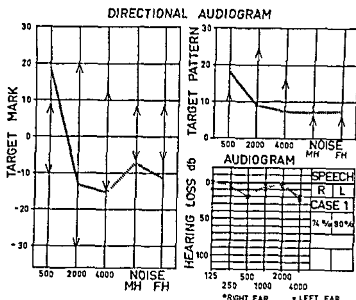


Fig. 7. Directional audiogram of a patient (No. 67) with a meningioma pontis sin. The tone audiogram is normal and the speech discrimination scores are almost normal. The abnormal target marks and target patterns indicate a probable lesion of the auditory nerve.

the 22 patients with cochlear lesions and the five patients with vestibular lesions. These 78 persons represent a group with no suspicion of lesions of the auditory nerve or the pons. Of them only cases 54 and 56 had one abnormal target pattern each. This occurred, as previously mentioned, when low-pass filtered white noise was presented with the head fixed. As can be seen in Table 1 the patterns were 6.3 and 7.1 respectively, thus just exceeding the normal limit. The target patterns of Patients 60–67 thus clearly differ from the above-mentioned persons. It is therefore clear that if no middle-ear lesion is present and *the hearing loss is not very asymmetrical, i.e. not more* than 50 db, an abnormal target pattern indicates a retrocochlear lesion. This is to some extent also true of the target mark. As can be seen in Table 3 the abnormal target patterns may occur before the speech discrimination scores became abnormal (Nos. 65, 60, 67, 66 and 61). It can also be seen that the abnormal target pattern may occur with a normal pure-tone audiogram (Nos. 62, 67, 63 and 61). In the clinic directional audiometry is thus *useful in the early diagnosis of retrochlear lesions.* Figs. 6 and 7 show directional audiograms in three cases. The method offers in this way a complement to recruitment tests, which are generally positive with cochlear lesions and negative with auditory nerve lesions. Directional audiometry on the other hand gives abnormal results with auditory nerve lesions and normal results with cochlear lesions.

An intact vestibular function is not necessary for a normal directional hearing, as previously shown by other investigators (for instance, Diamant, 1946, Koenig & Sussman, 1955). Unilaterally deaf patients have an impaired directional hearing, as is expected on theoretical grounds, since directional hearing is mainly a binaural function. Patients with brain lesions generally

have a normal directional hearing which is natural when the auditory path ways are not affected The investigation of directional hearing can therefore never be a method for detecting all kinds of brain lesions

In future the method probably can be simplified Already from these ob servations it seems that the 2000 cps signal does not furnish much informa tion

CONCLUSIONS

1 Directional audiometry is not correlated with pure tone or speech audio grams and thus offers additional information concerning auditory function

2 Patients with middle ear lesions often have impaired directional hearing

3 Patients with cochlear lesions have only slight impairment of direc tional hearing compared with normal subjects

4 Patients with lesions of the auditory nerve or the pontile region have markedly impaired directional hearing

5 Patients with brain lesions may have an entirely normal directional hearing unless the lower auditory pathways are affected

6 Normal vestibular function is not necessary for normal directional hea ring

7 Directional audiometry appears to be of great potential value for the diagnosis of auditory nerve lesions The change of target pattern, i e standard deviation of the differences between the true position of the loudspeaker and the position as judged by the subject is the most valuable diagnostic sign in evaluating directional hearing

ZUSAMMENFASSUNG

Das Richtungshoren von Patienten mit verschiedenen Arten von Gehorschaden wurde einer Untersuchung unterzogen, die den Wert der Richtungsaudiometrie als ein Hilfsmittel zur topischen Diagnose von Gehorverschlechterungen dienen sollte Die Metode der Richtungsaudiometrie ist in einer vorgehenden Abhandlung im Ein zelnen beschrieben worden In der vorliegenden Veroffentlichung wird das Ergebniss vom Messresultat an einundfunfzig normalhorenden Personen sowie von ein hundertein Patienten mit verschiedenen Gehorstorungen ausgewertet Es zeigt sich dabei dass Vermogen der Winkelabschatzung bei Personen mit Leitungsschaden leicht verringert ist Ebenso haben Patienten mit Innenohrschaden ein verhaltnis massig gut erhalternes Richtungshorvermogen Dagegen ist diese Fahigkeit bei Personen mit Schaden des Gehornerven oder der Pons verringert Die Richtungs audiometrie darf daher als eine wertvolle Methode zur Unterscheidung zwischen kochlearen und retrokochlearen Schaden betrachtet werden

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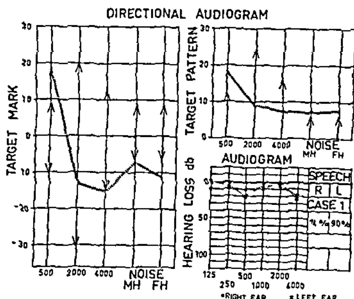


FIG 7 Directional audiogram of a patient (No 67) with a mening reg ang pont sin The tone audiogram is normal and the speech discrimination scores are almost normal The abnormal target marks and target patterns indicate a probable lesion of the auditory nerve

the 22 patients with cochlear lesions and the five patients with vestibular lesions These 78 persons represent a group with no suspicion of lesions of the auditory nerve or the pons Of them only cases 54 and 56 had one abnormal target pattern each This occurred, as previously mentioned, when low-pass filtered white noise was presented with the head fixed As can be seen in Table 1 the patterns were 6 3 and 7.1 respectively, thus just exceeding the normal limit The target patterns of Patients 60–67 thus clearly differ from the above mentioned persons It is therefore clear that if no middle-ear lesion is present and the hearing loss is not very asymmetrical, i e not more than 50 db, an abnormal target pattern indicates a retrocochlear lesion This is to some extent also true of the target mark As can be seen in Table 3 the abnormal target patterns may occur before the speech discrimination scores became abnormal (Nos 65, 60, 67, 66 and 61) It can also be seen that the abnormal target pattern may occur with a normal pure tone audiogram (Nos 62 67, 63 and 61) In the clinic directional audiometry is thus useful in the early diagnosis of retrocochlear lesions Figs 6 and 7 show directional audiograms in three cases The method offers in this way a complement to recruitment tests, which are generally positive with cochlear lesions and negative with auditory nerve lesions Directional audiometry on the other hand gives abnormal results with auditory nerve lesions and normal results with cochlear lesions

An intact vestibular function is not necessary for a normal directional hearing, as previously shown by other investigators (for instance, Diamant, 1946, Koenig & Sussman, 1955) Unilaterally deaf patients have an impaired directional hearing, as is expected on theoretical grounds, since directional hearing is mainly a binaural function Patients with brain lesions generally

BLUTGASÄNDERUNGEN NACH TRACHEOTOMIE BEI CHRONISCHEN TRACHEALSTENOSEN
DER ATEMSTILLSTAND NACH TRACHEOTOMIE

H. J. Nickol und D. Lerche
Hamburg und Berlin, Deutschland

Aus der Klinik für Hals-, Nasen- und Ohrenkrankheiten der Universität Hamburg (Direktor: Prof. Dr. Rud. Link) und der Cardiologischen Abteilung (Leiter: Priv.-Doz. Dr. Neuhaus) der I. Medizinischen Klinik der Freien Universität Berlin (Direktor: Prof. Dr. H. Frhr. von Kress)

Plötzlicher Atemstillstand mit letalem Ausgang tracheotomierter Patienten war der Anlaß zu gasanalytischen Untersuchungen des arteriellen Blutes und des Liquors. Vor, unmittelbar nach und 24 Stunden nach der Tracheotomie wurde bei Kranken mit hochgradiger Einengung des Kehlkopfes oder der Trachea die Arteria femoralis und der Lumbalkanal punktiert. Zwei Hunde mit experimentell gesetzten Trachealstenosen durch Einschieben von ineinander eingepaßten Plexiglaseinsätzen untermauerten die Ergebnisse. Ohne den Beweis antreten zu können, wird als Todesursache durch Atemstillstand eine verminderte Ventilation bzw. eine Verschiebung der Atemreizschwelle durch eine metabolische Alkalose infolge der chronischen respiratorischen Acidose und die langanhaltende CO_2-Wirkung auf das Atemzentrum mit Erhöhung der Reizschwelle angenommen. Als therapeutische Konsequenz wurde der verlorengegangene Totraum über der Stenose dadurch künstlich ersetzt, indem ein Gummischlauch von ca. 10 cm Länge in die Trachealkanüle eingeschoben wurde. Er wurde langsam durch Abschneiden gekürzt. Somit konnte ein zu schnelles Abrauchen des erhöhten CO_2 verhindert werden. Die medikamentösen Gaben von sauren Valenzen zum Beleben der metabolischen Alkalose wurde abgelehnt.

Bei Patienten mit hochgradigen chronischen Stenosen der Atemwege durch einen einengenden Prozeß im Bereich der Trachea macht der bedrohliche Zustand der Dyspnoe, Cyanose und die erhebliche Herzbelastung eine baldige Tracheotomie notwendig. Unmittelbar nach derselben fühlen sich die Patienten besser, weil der erhöhte Atemwiderstand behoben ist. Kurze Zeit später wird jedoch eine zunehmende Schläfrigkeit mit einem Nachlassen der Atmung beobachtet, wobei es häufig zu einem Atemstillstand und bisweilen zu einem letalen Ausgang kommt. Als Ursache wurde meist ein „Herz- und Kreislaufversagen" angenommen. Aber bereits Greene

Herrn Prof. Dr. H. Frhr. von Kress zum 60. Geburtstag gewidmet.
Mit Unterstützung der Deutschen Forschungsgemeinschaft.

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Sahlgrenska Sjukhuset, University of Goteborg Sweden

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experimenteller zunehmender Trachealstenose und nach Tracheotomie bei 2 Hunden, vor Narkose

Ph Blut			Ph Liquor			HCO_3 Blut (val/l)			HCO_3 Liquor (val/l)		
vor	nach	n 24^h	vor	nach	n 24^h	vor	nach	n 24^h	vor	nach	n 24^h
7 333	7 379					19 39	18 63				
7 420	7 610					30 3	20 69				
7 4 0						27 93					
7 [illegible]0	7 340	7 541	7 101	7 320	7 340	39 74	26 65	27 49			
7 382	7 445	7 480	7 338	7 435	7 300	26 50	22 96	27 04			
7 382	7 382	7 480	7 300	7 320	7 359	30 61	28 29	27 51	29 80	31 40	25 76
7 315	7 560	7 500	7,360	7 420	7 340	26 14	20 24	22 95	27 32	27 12	23 01
7 390	7 [illegible]		7 370	7 380		26 75	21 94		23 82	24 73	
7 460	7 495	7 459			7 360	25 04	21 78	21 67			21 73
7 3[illegible]5	7 361	7 513	7 290	7 292	7 317	25 94	19 67	24 73	25 81	23 91	23 78
[illegible]1	7 500	7 513	7 370	7 361	7 188	24 60	23 51	25 30	24 13	22 93	20,83
7 218	7 512					18 90	20 64				
7 418	7 410	7 481	7 [illegible]65	7 3[illegible]1	7 290	29 41	25 70	24 08	33 2	31 79	27 05

und von 38 auf 37° umgerechnet wurden Im arteriellen Blut wurden CO_2 Gehalt O_2 Gehalt und O_2 Kapazität und im Liquor CO_2 Gehalt mit der manometrischen Methode von van Slyke u Neill (1932) bestimmt

a) Berechnung der Blutwerte Aus O_2 Gehalt nach Abzug des physikalisch gelösten Sauerstoffs und O_2 Kapazität wurde die O_2 Sättigung des arteriellen Blutes errechnet Aus CO_2 Gehalt des Blutes ph und O_2 Kapazität wurde mit dem Nomogramm von van Slyke u Sendroy (1928) der CO_2 Gehalt des Plasmas berechnet Hieraus und aus dem Blut ph wurden der CO_2 Druck und das aktuelle Bikarbonat des arteriellen Blutes mit der Henderson Hasselbalch schen Gleichung (1932) unter Berücksichtigung des von Severinghaus (1956) angegebenen pk Diagramms errechnet

b) Berechnung im Liquor cerebrospinalis Aus CO_2 Gehalt und ph im Liquor wurde mit der Henderson Hasselbalch schen Gleichung der CO_2 Druck errechnet wobei S mit 0 0323 eingesetzt und pk aus dem ph pk Diagramm von Schwab abgelesen wurde (1962) Das aktuelle Bikarbonat wurde ebenfalls nach Hasselbalch Henderson errechnet

Ergebnisse beim Menschen

In Abb 3 sind die arteriellen CO_2 Druckänderungen aller Patienten vor und unmittelbar nach Tracheotomie und nach 24 Stunden aufgetragen 7 von den 13 Patienten liegen vor der Tracheotomie mit ihren arteriellen PCO_2 Werten im pathologischen Bereich (Norm 39 9 Torr (36 2–44 9) (Katsaros u a, 1960)) während 2 Patienten CO_2 Druckwerte zwischen 36 und 45 Torr aufweisen Somit liegt bis auf 2 Fälle der arterielle CO_2 Druck

TABELLE 1 *O_2 Sättigung, Ph CO₂ Druck und aktuelles Bicarbonat im arteriellen Blut b*
und

Patienten	SO_2 (%) vor	nach	n 24[h]	PCO_2 Blut (Torr) vor	nach	n 24[h]	PCO_2 Liquor (Torr) vor	nach	n 2
Weibl 79 J	91	91		32 37	31 61				
Weibl 56 J	67 5	71		45 5	19 9				
Weibl 51 J	56	85		37 78					
Männl 62 J	68	81	87	68 41	49 12	31 63			
Männl 68 J	94	87	91	44 22	32 93	35 71			
Weibl 70 J	74	87	87	51 08	47 21	36 35	62 9	63 1	4
Weibl 75 J	88	95	97	17 60	22 02	28 75	49 8	42 1	43
Weibl 52 J	92	92		40 58	31 20		47 8	45 1	
Weibl 62 J	97	92	91	34 81	27 60	30 13			39
Weibl 79 J	77	89	88	49 76	31 55	30 19	55 6	51 3	47
Männl 75 J	96	96	90	39 74	25 63	30 88	42 9	41 7	5
Weibl 43 J	83	82		47 3	25 1				
Männl 64 J	59	69	85	45 3	10 2	31 7	51 2	48 8	3

(1959) wies auf Kollapszustände nach Tracheotomie hin und machte das plötzliche Absinken des Kohlensäuredruckes dafür verantwortlich.

Die Frage, ob es sich bei diesen Erscheinungen um ein Versagen des Atemzentrums durch den plötzlichen CO_2 Abfall handelt, blieb bislang ungeklärt. Wir stellten uns daher die Aufgabe, Patienten, die in die hiesige Hals-Nasen-Ohrenklinik mit hochgradigen Stenosen eingewiesen wurden, vor und nach Tracheotomie gasanalytischen Blut- und Liquoruntersuchungen zu unterziehen.

Ferner sollten in Experimenten am Hund durch künstliche Stenosen der Atemwege vergleichbare Veränderungen geschaffen und untersucht werden.

Methodik beim Menschen

Untersucht wurden insgesamt 20 Patienten, von denen 7 lediglich Vorversuchen unterzogen wurden und daher nicht in der Tabelle 1 erscheinen. Bei 13 Patienten wurde unmittelbar vor der Tracheotomie und etwa 10 Minuten danach eine Arterienpunktion und bei einigen eine Lumbalpunktion durchgeführt. Die gleichen Untersuchungen wurden 24 Stunden später wiederholt. Das arterielle Blut wurde in Rückenlage aus der A. femoralis entnommen, während der Liquor cerebrospinalis in Seitenlage aus dem Lumbalsack abpunktiert wurde. Die Entnahmen erfolgten streng anaerob unter Zusatz von Heparin und Natriumfluorid in siliconisierten Glasspritzen.

Wir bestimmten das ph mit dem Philips-Meter in einer Schottglaselektrode nach vorheriger Eichung mit Sorensen Phosphatpuffern von ph 7 367 und 7 704 bei 37°, wobei die Angaben von Hastings u. Sendroy (1924) verwendet

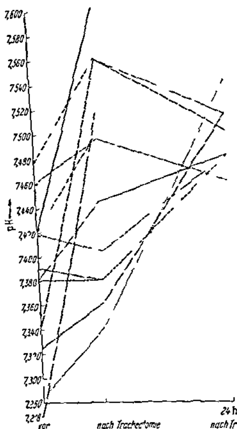


Abb. 2. Änderung der arteriellen Wasserstoffionenkonzentration bei 12 Patienten mit Trachealstenose vor und nach Tracheotomie sowie 24 Stunden später

cheotomie ab. Bei Vergleich mit den Blutwerten lag der CO_2-Druck im Liquor bei allen Bestimmungen höher. Die Differenz Liquor PCO_2 zu Blut PCO_2 betrug 2 2 11 Torr vor der Tracheotomie, während nach der Tracheotomie eine eindeutige Zunahme der Differenz beobachtet wurde. Auch noch nach 24 Stunden lag der Liquor-CO_2-Druck über den Blutwerten. Die ph-Werte im Liquor wiesen vor der Tracheotomie nicht so starke Streuungen auf wie im Blut. Nach der Tracheotomie trat bei allen 8 Untersuchungen eine Verschiebung zur alkalischen Seite auf. Bei Vergleich mit den Blutwerten lag bei fast allen Untersuchungen die Wasserstoffionenkonzentration im Liquor höher, wobei die Differenz Blut ph zu Liquor ph nach 24 Stunden am größten war.

Methodik der Tierversuche

Versuchstiere waren 2 ausgewachsene Hunde von 22 und 18 kg. Um einen Vergleich zu den Befunden beim Menschen zu haben, mußte die Trachea

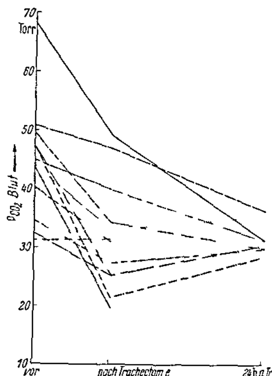


Abb. 1. Arterielle CO_2-Druckänderung bei 12 Patienten mit Trachealstenose vor und nach Tracheotomie sowie 24 Stunden später.

vor der Tracheotomie außerhalb des physiologischen Bereiches. Unmittelbar nach der Tracheotomie kommt es bei allen Fällen zu einem Absinken des arteriellen CO_2-Druckes, wobei z. T. Werte erreicht werden, die weit unter dem physiologischen Bereich liegen. Bei einigen Patienten ist der CO_2-Druck noch über der Norm. 24 Stunden später zeigt sich bei allen Fällen eine Tendenz zur Normalisierung.

Die pH-Werte (Abb. 2) vor der Tracheotomie zeigen eine große Streuung nach der sauren und alkalischen Seite, weisen aber nach der Tracheotomie entsprechend der CO_2-Druckänderung eine eindeutige Verschiebung nach der alkalischen Seite auf. Je alkalischer der Ausgangswert, desto größer ist die anschließende Alkalose, die aber nicht mit einem stärkeren Absinken des PCO_2 parallel geht. Im Gegensatz zu dem Hang der Normalisierung des arteriellen PCO_2 liegen nach 24 Stunden die pH-Werte weiterhin im alkalischen Bereich und werden auch von Patienten erreicht, die unmittelbar vor der Tracheotomie normale pH-Werte aufwiesen. Die aktuellen Bikarbonatwerte liegen vor, nach Tracheotomie und 24 Stunden später alle bis auf einen herausfallenden Wert im Normbereich. Die arterielle Sättigung, die bei den meisten Patienten vor Tracheotomie erheblich vermindert war, zeigte nach Tracheotomie eine deutliche Besserung.

Der CO_2-Wert im Liquor cerebrospinalis lag vor der Tracheotomie bei allen Patienten über der Norm, wenn auch die Werte erheblichen Streuungen unterworfen waren, und sank bei [illegible] Patienten unmittelbar nach der Tra-



Abb 3 Operativ angelegte Carotisschlingen

langsam zunehmend eingeengt werden Auf Punktionen des Liquor cerebrospinalis mußte wegen der geringen Liquormenge beim Hund verzichtet werden

Bei dem ersten Hund erfolgte in erster Sitzung nach medikamentoser Vorbereitung mit Megaphen in Polamivet Narkose die Anlegung der Carotisschlinge links (Abb 3)

Bei der Anlegung der rechten Carotisschlinge 3 Wochen spater wurde ein Plexiglaseinsatz der entsprechend der Große der Trachea angefertigt worden war durch die in Hohe der 5 Trachealschlinge quer eroffnete Trachea bis unter die Stimmbander eingeschoben und mittels 4 kleiner Schrauben fixiert (Abb 4 5 und 6)

Die Operationen erfolgten unter Antibiotikaschutz Die Wunden sowie die Carotisschlingen wurden durch einen Watte Starke Kragenverband geschutzt Nach Abheilung trug der Hund eine ausreichend breite Ledermanschette um den Hals Nach 4 Wochen wurde unter Megaphen in Pola

TABELLE 2 *O_2 Sättigung, Ph, CO_2 Druck und aktuelles Bicarbonat im arteriellen Blut bei experimenteller zunehmender Trachealstenose und nach Tracheotomie bei 2 Hunden, vor und in Narkose*

P = nach Einsetzen eines Plexiglasrohres v (vor) und n (nach) T (Tracheotomie) v (vor) und n (nach) E (Einsatz eines Tubus in die Trachealkanüle) Siehe Text

SO_2 arteriell (%)		PH arteriell		PCO_2 arteriell		HCO_3 aktuell	
vor Narkose	in Narkose	vor Narkose	in Narkose	vor Narkose	in Narkose	vor Narkose	in Narkose
90	76	7,405	7,290	12,73	15,27	20,73	21,70
98	P = 93	7,135	P = 7,320	29,86	P = 11,32	20,31	P = 22,83
98	P = 88	7,123	P = 7,360	31,26	P = 35,09		P = 19,91
	94		7,360		39,87		22,66
92		7,102		31,52		19,80	
	71	7,147	vT = 7,371	28,97	vT = 39,50	20,26	vT = 23,29
100	vT = 86		7,390		20,97		10,63
	nT = 85						
21^hnT = 100		21^hnT = 7,156		21^hnT = 28,26		21^hnT = 20,21	
100	vT = 93	7,190	vT = 7,360	21,33	vT = 41,51	18,86	vT = 25,29
	nT = 97		nT = 7,396		nT = 36,51		nT = 22,61
	I = 85		I = 7,340		I = 40,28		I = 21,76
	II = 92		II = 7,260		II = 19,26		II = 21,93
	III = 84		III = 7,290		III = 12,91		III = 20,52
	P = 92		P = 7,599		P = 21,15		P = 21,31
	81		7,379		31,21		20,35
	92		7,310		41,70		21,70
	P = 92		P = 7,359		P = 38,80		P = 22,06
	96		7,326		12,65		22,28
	vT 67		vT = 7,322		vT = 58,26		vT = 23,96
	5'nT 79		5 nT = 7,399		5'nT = 32,95		5'nT = 20,51
	15'nT 80		15 nT = 7,529		80'nT = 24,02		15'nT = 20,88
	21^hnT 91		21^hnT = 7,380		21^hnT = 33,12		21^hnT = 19,71
	vT 92		vT = [illegible]		vT = [illegible]		



Abb. 6. Plexiglaseinsatz in der Trachea eingeheilt (Schrauben durch Pfeil gekennzeichnet)

sentlichen Störungen. Auch das Bellen der Hunde war noch praktisch normal. Nach weiteren 4 Wochen wurde auf gleiche Weise der 3. Einsatz eingeschoben, ebenfalls unter Kontrolle der Blutgaswerte des arteriellen Blutes aus der Femoralis. Der letzte Einsatz mit einem Durchmesser von 5 mm erfolgte nach abermals 4 Wochen und wurde 7 Wochen belassen (Abb. 6).

Dabei trat eine leichte Atemnot in Ruhe und eine deutliche Dyspnoe bei Belastung auf. Vor der Tracheotomie wurden je eine Arterienpunktion vor und in Narkose durchgeführt. Unmittelbar nach der Tracheotomie sowie 1 Stunde später und nach 24 Stunden erfolgte eine erneute Arterienpunktion der Carotisschlinge. Nach 2 Tagen wurde bei dem ersten Versuchstier die Kanüle entfernt und nach 4½ Wochen unter derselben Versuchsanordnung erneut eingelegt. Unmittelbar nach der letzten Arterienpunktion wurde der Hund ausgeblutet und Gehirn, Herz, Leber und Nieren zur histologischen Untersuchung entnommen. Nach Isolierung der Trachea mit Kehlkopf



Abb. 4. Seitenansicht der Plexiglaseinsätze: größter und kleinster Einsatz

unter Narkose mittels direkter Laryngoskopie der nächste Einsatz eingeschoben und mit UHU-Klebestoff fixiert. Vor und unmittelbar nach dem Einbringen des zweiten Plexiglasrohres wurde arterielles Blut zur Blutgasanalyse entnommen. Der vorübergehende Husten konnte durch Kodein beseitigt werden. Mit diesem zweiten Einsatz zeigte der Hund noch keine we-

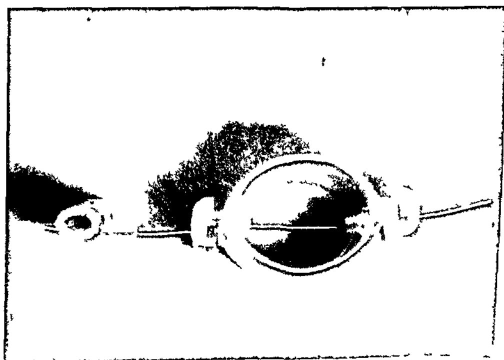


Abb. 5. Aufsicht der Plexiglaseinsätze: größter und kleinster Einsatz

eine im Durchmesser kleinere Plexiglasrohre trug mit einem PCO_2 von 58 Torr außerhalb der physiologischen Streubreite Nach der Tracheotomie kommt es zu einem deutlichen Absinken des CO_2 Druckes wobei der Abfall bei dem hochsten Ausgangswert am großten wird Wird beim gleichen Versuchstier erneut die Stenose angelegt ist bei Wiederholung der Tracheotomie der arterielle PCO_2 Abfall nicht mehr so ausgepragt Bei dem zweiten Versuchstier wurde wie beschrieben nach der Tracheotomie eine Trachealkanule angelegt und mit einem Tubus eine Verengerung herbeigefuhrt Wird hier nach einer Gewohnungszeit der Tubus entfernt so kommt es nicht zu einer wesentlichen Änderung des arteriellen PCO_2 oder ph

Zum histologischen Nachweis hypoxamischer Schaden wurde die Medulla oblongata im Bereich der Formatio reticularis seriengeschnitten eingehend untersucht besonders die caudalen Gebiete der Rautengrube mit den Zentren der Atmung und der Kreislauforgane Typische Veranderungen mit Zelluntergang konnten hier ebenso wenig festgestellt werden wie Sauerstoffmangelschaden in den Präparaten des Herzens der Leber und der Niere

DISKUSSION

Bei einem relativ kleinen Patientenmaterial mit verschiedenen Graden von Trachealstenosen und entsprechend unterschiedlichen Werten kann eine Verallgemeinerung nur mit Vorbehalt geschehen Unter der chronischen Trachealstenose kommt es zu einem Anstieg des arteriellen CO_2 Druckes der in seiner Hohe unter anderem vom Grad der Stenose und der Diffusionsfahigkeit der Lunge abhangig ist Die blutgasanalytischen Werte konnen als Ausdruck einer respiratorischen Acidose angesehen werden wobei es sich um eine alveolare Hypoventilation und nicht um eine zentrale Atemregulationsstorung handelt Je ausgepragter die Stenose desto niedriger liegt der Atemgrenzwert d h desto kleiner ist das Atemzeitvolumen Hinzu kommt wahrscheinlich noch eine reflektorische Umstellung der Atmung (Kleinsorg 1959) wobei Julich (1960) annimt daß die sensiblen Pressorezeptoren der Pleura sowie Lungen bei Stenoseatmung gereizt werden und ihrerseits uber den Nervus vagus das Atemzentrum beeinflussen Ferner spielt eine gewisse Ermudung der Atemmuskulatur durch die erhohte Atemarbeit eine Rolle (Kleinsorg u Kochsiek 1959)

Unter dieser Hyperkapnie tritt wie bekannt ein Anstieg der peripheren und zentralen Durchblutung und ein Anstieg des Liquordruckes auf Die chronische respiratorische Acidose versucht der Organismus soweit wie moglich mit einer metabolischen Alkalose zu kompensieren Die Gegenregulation muß aber bei einem Weiterbestehen der Stenose unzureichend sein Durch Ruckresorption von HCO_3 in den Nieren wird das ph zwar nach der alkalischen Seite verschoben und damit der CO_2 Druck etwas niedriger liegen die Acidose jedoch weiter bestehen

Bei fehlender oder nur geringer Trachealstenose kommt es bei der Tracheotomie allein durch die Verkleinerung des Totraumes schon zu einem

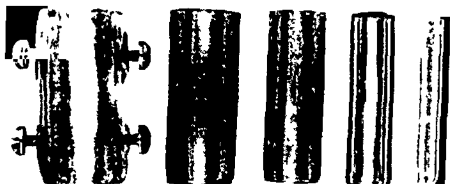


Abb 7 Plexiglaseinsätze

Kehldeckel und Zunge zeigte sich, daß der Plexiglaseinsatz ohne wesentliche entzündliche Reaktionen der Umgebung eingeheilt war

Bei dem zweiten Versuchstier wurden die gleichen operativen Eingriffe vorgenommen, wobei jedoch die Carotisschlingen und das Einbringen des ersten und zweiten Einsatzes mit entsprechender Blutgasanalyse vor und nach dem Eingriff in einer Sitzung erfolgte Der kleinste Einsatz hatte einen Durchmesser 2/1 mm (Abb 7) und konnte wegen der hochgradigen Atemnot nur 48 Stunden bis zur Tracheotomie belassen werden Nach Tracheotomie und Einsetzen einer Trachealkanule trat im wachen Zustand eine erhebliche Unruhe verbunden mit Hyperventilation und Tachycardie auf Diese ließ nach Einschieben eines Gummitubus in die Trachealkanule zwecks Einengung wieder nach Wurde der Tubus jedoch wieder entfernt trat eine erneute Hyperventilation auf Er wurde daher 14 Tage belassen und in Narkose bei den beschriebenen Kontrollen entfernt Auch hier zeigte das Sektionspräparat eine völlige reizlose Einheilung der Plexiglaseinsätze

Ergebnisse der Tierversuche

In Übereinstimmung mit Albers u a (1959) kam es bei beiden Versuchstieren durch die Narkose zu einem Anstieg des arteriellen PCO_2 während entsprechend das ph nach der sauren Seite abwich Daher sind nur die Werte innerhalb der Narkose als vergleichbar anzusehen Der bekannte Abstieg und Abfall der arteriellen PCO_2 unter Narkose ist deutlich, liegt aber noch im physiologischen Bereich Besteht eine chronische Trachealstenose, liegen die Werte beim Hund 1 innerhalb der Norm, aber bei I

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Abb 8 Trachealkanüle mit Gummischlauchansatz

Die metabolische Stoffwechsellage kann besser durch dosierte CO_2 Anreicherung ausgeglichen werden Wird nach der Tracheotomie in die Trachealkanüle ein angepaßter Gummischlauch (Abb 8) eingebracht so kann damit über die Totraumvergrößerung auch die alveoläre bzw arterielle CO_2 Spannung erhöht werden Da CO_2 die Zellmembranen schneller durchdringt ist der intra extrazelluläre ph Gradient relativ rasch wieder normalisiert Nach unseren Erfahrungen die allerdings noch entsprechender Kontrolluntersuchungen bedürfen genügt ein etwa 10 cm langer Gummischlauch mit einem Durchmesser von etwa 1 cm der im Laufe von 1 2 Tagen mehrmals um 2 3 cm gekürzt wird

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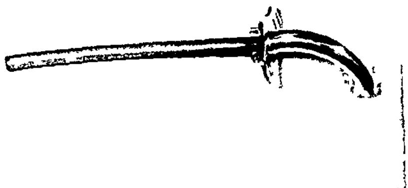


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ON HYALURONATE MOLECULES IN THE LABYRINTH AS MECHANO-ELECTRICAL TRANSDUCERS AND AS MOLECULAR MOTORS ACTING AS RESONATORS

J. A. Christiansen
Hellerup, Denmark

Part I contains a discussion of the significance of displacement potentials as caused by the bending of hyaluronate molecules, for the understanding of the electrical phenomena in the vestibular apparatus. It appears that the conclusions drawn from their existence and from their theory agree in sign and in order of magnitude with effects demonstrated experimentally in the organ of the semicircular canals, notably by Trincker and by Lowenstein & Wersall. But it seems that we are left with a choice of at least two possible mechanisms.

In part II the considerations are extended to an attempt to understand the electrical phenomena which are characteristic for the cochlea. In particular it is attempted to explain the supposedly peripheric analysis of sounds in respect of pitch. The principal point of view is that due to Helmholtz (1863): the analysis must be explained by means of some sort of resonator mechanism combined with the so called place theory. In contrast to Helmholtz's views, however, the resonators are believed to be molecular motors having a characteristic frequency of rotation and not vibrators *of the* violin string type.

It is shown that, when certain conditions obtain, bent hyaluronate molecules act as electrical switches and as *revolving motors* with a *characteristic* frequency of rotation. *It is also shown* that the experiments by Galambos & Davis and by Tasaki do not necessarily disprove the proposed mechanism. On the contrary, it may seem that the mechanism in question must lead to consequences like those observed by *the said authors* on single nerve fibres.

It is often assumed that the electrical changes, which stimulate the nerve endings *in the sensory cells of the* labyrinth, are cause[illegible]

[illegible] *deformations of* much smaller structure elements, bendings of *thread like* molecules. An important class of such molecules is the one of *mucopolysaccharides*, which includes the hyaluronic acids and their salts, *of which we shall* make extensive use in the following.

I. *Application of Displacement Potentials to the Vestibular Apparatus*

The idea that hyaluronate molecules play an important role in the function of the vestibular apparatus is due to Th. Vilstrup. In 1953 Jensen & Vilstrup

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Oberarzt Dr H J Nickol, Univ HNO Klinik
Hamburg, Martinistr 52, Deutschland

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ON HYALURONATE MOLECULES IN THE LABYRINTH AS MECHANO-ELECTRICAL TRANSDUCERS, AND AS MOLECULAR MOTORS ACTING AS RESONATORS

J A Christiansen
Hellerup, Denmark

Part I contains a discussion of the significance of displacement potentials, as caused by the bending of hyaluronate molecules, for the understanding of the electrical phenomena in the vestibular apparatus It appears that the conclusions drawn from their existence and from their theory agree in sign and in order of magnitude with effects demonstrated experimentally in the organ of the semicircular canals, notably by Trincker and by Lowenstein & Wersall But it seems that we are left with a choice of at least two possible mechanisms

In part II the considerations are extended to an attempt to understand the electrical phenomena which are characteristic for the cochlea In particular, it is attempted to explain the supposedly peripheric analysis of sounds in respect of pitch The principal point of view is that due to Helmholtz (1863), the analysis must be explained by means of some sort of resonator mechanism combined with the so called place theory In contrast to Helmholtz s views, however, the resonators are believed to be molecular motors, having a characteristic frequency of rotation and not vibrators of the violin string type

It is shown that, when certain conditions obtain, bent hyaluronate molecules act as electrical switches and as revolving motors with a characteristic frequency of rotation It is also shown that the experiments by Galambos & Davis and by Tasaki do not necessarily disprove the proposed mechanism On the contrary, it may seem that the mechanism in question must lead to consequences like those observed by the said authors on single nerve fibres

It is often assumed that the electrical changes, which stimulate the nerve-endings in the sensory cells of the labyrinth, are caused by mechanical deformations of the cells and particularly by bending of their hairs

The leading idea in the following is that, in order to understand the phenomena in question, we must consider deformations of much smaller structure elements bendings of thread like molecules An important class of such molecules is the one of mucopolysaccharides, which includes the hyaluronic acids and their salts, of which we shall make extensive use in the following

I Application of Displacement Potentials to the Vestibular Apparatus

The idea that hyaluronate molecules play an important role in the function of the vestibular apparatus is due to Th Vilstrup In 1953 Jensen & Vilstrup

(1) showed them to be present in the endolymph of sharks The collaboration of these two authors continued until Jensen died in November 1959 One of their last joint papers, where references to the earlier ones are to be found, appeared in 1960 (2) One of the results of this cooperative work was that hyaluronate usually, and probably always, is a component of the substances in the hair zones of the inner ear

Vilstrup's idea was discussed and corroborated in contributions to the Oto-laryngological Colloquium at Padova in 1960 (3) by Vilstrup & † Jensen (4), by the present author (5) and by colleagues taking part in the symposium

The views set forth in the papers just quoted are based on an experimental fact, discovered by Jensen, Koefoed & Vilstrup (6) A displacement of a column of a solution of potassium hyaluronate in a glass capillary produces an electric potential difference in the column They found that the end of the column which is foremost in the direction of displacement becomes the positive one This potential has been given the name "displacement potential" to distinguish it from "streaming potential" The characteristic difference between these two kinds of potentials is that, while the latter decays practically instantaneously when the movement stops, the former subsists or decays very slowly so long as the column is maintained in its displaced position The displacement potential is independent of the distance between the electrodes by which it is measured, so far as observations go

The phenomenon can be understood as being due to a bending of the threadlike hyaluronate molecules Calculations by the present author (7) on a simplified model of the molecule yielded results which agreed qualitatively, and reasonably well quantitatively, with experience The potentials turned out, experimentally, to be of the order of 10 mV, but under circumstances where most of the molecules could be expected to adhere to the glass wall with one end they would rise to higher values, to about 100 mV Also this effect could be explained by the theory (7) It is a consequence of the theory that the potential has a lower limiting value different from zero for a given length of the molecules Both effects seem to be verified by the measurements of Trincker (8 9) on the vestibular system

The first attempt to understand the electrical effects on the sensory cells of the inner ear was made with the cells on the cristae of the semicircular canals It is known that, in the ampullae of these, the movements of the subcupular substance must be parallel to the surface of the crista and therefore perpendicular to the sensory hairs It was further known experimentally, that a displacement of the cupula with its subcupular substance in one direction caused a depolarisation of the interior of the sensory cell, ensuing in an increased activity in the nerve fibre in question, while a displacement in the opposite direction caused the opposite effects This directional effect could *not* be interpreted as an effect of potentials caused by displacements transversal to the hairs, because it was then believed that the hairs were arranged symmetrically on the free surface of the cell This negative result was the outcome of repeated oral discussions between Professor Dohlman

and the author. However, about at the same time Wersäll (10) and Engström (11) discovered by means of the electron microscope that the arrangement was not at all symmetrical. They found that one single hair, the kinocilium, is completely different from all the others, the stereociliae, on the same cell. There are about 70 stereociliae on one cell, and the kinocilium is located as unsymmetrically as possible relative to the group of stereociliae. As can be seen from a photograph by Wersäll (10), Fig. 3, the stereociliae are arranged in a characteristic pattern. After that Löwenstein & Wersäll (12) found firstly that the kinociliae on different cells belonging to the same crista (of the ampulla of a semicircular canal) are all orientated in the same way relative to the corresponding groups of stereociliae. Secondly they found that a displacement of the subcupular substance in the direction from the stereociliae to the kinocilium causes a depolarisation of the interior of the cell, resulting in an increase in its spontaneous activity. These discoveries make it possible to understand the behaviour of the cell. For example, one may suggest the following mechanism. A displacement of the subcupular substance towards the kinocilium *must produce a potential tending to chase* positive electricity into the surroundings of the kinocilium. This must cause a movement of negative electricity from the bulk of the cell into its kinocilium, thus producing a depolarisation of the negative interior of the cell. Evidently a displacement in the opposite direction must cause the opposite effect, an increase of the negativity of the interior of the cell. For this mechanism to work a circumstance, whose importance has been stressed by Dohlman (13), is essential. The surface area of the hair bearing end of the cell *with the hairs can be estimated to* 2000–4000 μ^2. The surface of the rest of *the cell is at most* 200–300 μ^2. If therefore both kinds of ciliae act as electric condensers, the capacity of the "stereocondensor" *must be* many times larger than that of the "kinocondensor". *This implies that* displacement of electrical charges inside the cell must cause potential variations *in the bulk of the cell* plus the kinocilium, while the potential difference across the membranes of the stereociliae must remain small.

It may not be literally true that the membranes of *the cell and* its hairs are insulators. But it is known that the *cell membrane* proper, and probably also the hair membranes, act as transporters *of electricity*, thereby maintaining the potential difference between the surroundings and the inside of the cell as if the membranes were insulators. Further *attention* should be drawn to a remark by Löwenstein (14) suggesting that an amplifier effect may be necessary for the understanding of the actual electr*ical effects*. He arrives at this suggestion from the assumption that the transducer operates through a piezo electric mechanism. Now, pressure variations which can occur inside the ampullae can only *produce piezo* electric potentials which have orders of magnitude less than those *actually observed* in the vestibular system, e.g. by Trincker (8). A piezo electric mechanism would therefore certainly require an amplifying effect. *But the situation* becomes entirely different when it is assumed that the transducer effect *is due to* displacement potentials

That kind of potentials is of the same order of magnitude as those actually observed However, even on the latter assumption, an amplifying effect may eventually prove necessary In that case one may imagine that the displacement potential acts as a grid voltage governing an electric current passing from the outside through the membrane of the kinocilium into the inside of the cell However, owing to lack of information it is at present impossible to decide which one of the two mechanisms, the "condensor mechanism" or the 'amplifier mechanism', is in better agreement with experiments

Location of the Hyaluronate Molecules

In the preceding paragraphs nothing has been said of the arrangement of the hyaluronate molecules relative to the sensory hairs However, it soon became evident that it is much easier to explain the situation, e g to an audience, when it is assumed that the molecules are fixed at one end to the surface of the hairs, much like the brush hairs on a pipe cleaner or a bottle cleaner Therefore this picture was adopted as a helpful didactic tool, but during the further development, the same picture proved to be a valuable working hypothesis To the author s knowledge there is no direct evidence favouring this hypothesis except the fact that the interspaces between the hairs are of the same order of magnitude as that of the estimated lengths of hyaluronate molecules, about half a micron at most Dohlman (13) estimates the diameter of the hairs to be about 0 4 μ and the interspaces to be about the same or a little less Several micrographs for example those of Bairati (15), Fig 3, Wersall (10), Fig 4, and Engstrom (11) Fig 6 would seem to indicate that the interspaces are rather the double of the diameters On the other hand, other pictures e g one by Wersall (10) Fig 3 confirm Dohlman s estimate For people who, like the present author, have no experience themselves of electron micrography it is impossible to estimate how and to what extent preparations may have been distorted by the cutting process and by shrinking in drying

However, in the following we shall assume the hypothesis concerning the brush hair like arrangement of the hyaluronate molecules on the sensory hairs to be valid

It should be added that, so far as can be seen it will not make much difference to the admittedly crude theory to be presented in the following if it is supposed that the molecules are embedded in a jelly surrounding the hairs In this connection attention should be drawn to a paper by Hvidberg & Jensen (16) on mucopolysaccharides in the connective tissue in the skin of mice From their Table 2 the present author has estimated that there are in the tissue 400 to 500 molecules of protein for each molecule of mucopolysaccharide

Transversal and Longitudinal Movements

We have hitherto considered only displacements of the surroundings of the hairs transversal to their axes For such displacements hyaluronate mole

cules which are fixed at one end to the hairs must produce potentials tending to move positive charges in the direction of the displacement. Therefore also if we accept the brush hair like arrangement of the molecules some sort of asymmetric arrangement of the hairs on the "lid" of the cell is necessary to make the cell direction sensitive. As we know, nature has achieved this by the asymmetric location of the kinocilium.

It may however also be of interest to consider displacements which are longitudinal relative to the hairs.

If we adopt the hypothetical brush like arrangement of the molecules on the hair it is obvious that a displacement against the cell, a downward displacement, must bend the molecules downwards and thereby produce a potential tending to chase positive charges into the bulk of the cell, that is, cause a depolarisation, while an upward displacement must cause a hyperpolarisation. (It must be borne in mind that for hydrodynamic reasons longitudinal movements are only possible at some distance from the "lid", that is, at the upper ends of the hairs.) Therefore to register up and down displacements the asymmetric arrangement may not be necessary.

In this connection an oral communication by S. H. Mygind to the author should be mentioned. He points out that not only the physiological effects of horizontal accelerations but also those of vertical accelerations should be explainable by the theory.

II. *Application of the Theory of Bent Hyaluronate Molecules to the Cochlea*

We apply the hypothesis of the brush like arrangement of the hyaluronate molecules on the hairs to the sensory cells of the cochlea also.

Calculations (7) on a crude model of a hyaluronate molecule gave the following results. If the molecule is fixed perpendicularly to a solid base, e.g. to a sensory hair, and if it is bent through a right angle, a potential difference will be created between the concave and the convex side of the bent hair. This electromotive force tends to chase positive electricity from the convex to the concave side, that is, in the direction of the displacement which caused the bending. In other words, we expect to observe a displacement potential. Its numerical value turned out to be

$$E = 1.833 \times 10^{-4}/aN \text{ mV} \qquad (1)$$

In equation (1) a means the radius in cm of the molecule supposed cylindrical and N the number of units in the molecule. Each of these units carries a negative elementary charge belonging to the core of the molecule and on its outside a positive ion, e.g. a potassium ion. Acceptable values are $a = 2.5 \times 10^{-8}$ cm and $N = 1000$. Inserting these in (1) we get

$$E = 7.3 \text{ mV}$$

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bent through a right angle But only the former type type 1 will act as an electric switch while the other one type 2 is impermeable or nearly so to protons at its free end Therefore it cannot act in that way whether bent or not

It is tempting but at present completely unwarranted by experience to surmise that the molecules on the sensory hairs in the cristae of the ampullae are of type 2 Nevertheless whether both types exist or not in the inner ear, we shall assume in the following admittedly with the same lack of direct evidence that the molecules on the hairs of the cochlear sensory cells are of type 1 Following Hallowell Davis (17 18) let us now consider the situation in the organ of Corti The sensory cells are located in the basilar membrane their lids being nearly flush with its upper surface and their hairs protruding into the tectorial membrane The latter one is in close contact with the scala media which contains endolymph It is an important fact that the endolymph in the scala media is positive by about 80 mV relative to the surrounding perilymph On the other hand the interior of the sensory cell is as is usual for cells negative by about 60 mV relative to the perilymph Therefore if we suppose the tectorial membrane to be at the same potential as the endolymph in the scala media which we probably must there is a potential difference of about 140 mV across the membrane of the hairs This potential difference tries to chase positive electricity from the scala media into the hairs and from there to the interior of the sensory cell

How these potentials are maintained is still an open question but one thing seems certain they must be maintained at the expense of chemical energy from enzymically catalysed chemical reactions probably metabolic reactions The source of the 60 mV is most probably located in the cell membrane and perhaps in the ciliar membranes For the localisation of the source of the 80 mV we have to choose between two guesses It may be located *either in* Reissner s membrane or in stria vascularis Simply because the latter is so much better provided with blood vessels than the former is it seems natural to assume that stria vascularis is the site for the electric generator but the question can hardly be considered settled as yet In the following we shall adopt the latter possibility It may now be recalled that the insides of the hairs are connected with their surroundings through molecular switches as described before *If the molecules are straight no current will* pass but if they become bent the switches are on and a current must pass through the membrane This must cause a depolarisation of the cell If a sufficient amount of electricity has leaked in this will release one or several action potentials (spikes) into the nerve fibre ending in the cell in question The bending of the molecules can be effected by movements of the basilar membrane relative to membrana tectoria In his investigations v Békesy (19) p 441 has demonstrated that sounds impinging on the eardrum cause such movements

We thus arrive at a mechanism which is very similar to that described by Davis (17) The travelling waves in the basilar membrane cause openings

in sufficient agreement with values for displacement potentials determined by experiments

But the calculations disclosed furthermore that when the molecule is bent through a right angle its negative core takes up one positive elementary charge Chemically this must mean that the bending compels the molecule to take up one proton from the surrounding water One may imagine the rest of the water molecule the negative hydroxyl ion to be placed at the centre of curvature of the bending thus visualising the direction of the electromotive force the displacement potential Inside the core the proton neutralises one of its *N* negative carboxylate groups transforming it into a carboxyl group

This must have an important consequence In a solution of an acid in water protons exist in the form of hydroxonium ions H_3O^+ (hydrogen ions) Placed between electrodes at different potentials such ions will give rise to an electric conductivity not so much because they *migrate* as a whole but because the protons are continually jumping from one water molecule to one of its neighbours We have every reason to believe that when a proton by the bending of a hyaluronate molecule has been forced into its core it will behave much like a proton in water Not only may it jump from one carboxyl group to a neighbouring carboxylate group but in between those there are a number of other basic groups notably hydroxyl groups at which it can take a temporary rest in its jumping *In other words the bending of* such a molecule will in all probability create a conductivity along its core a conductivity which disappears when the molecule is unbent

To enter the core the proton must follow the easiest path The sheath of positive ions surrounding the negative core must produce a potential barrier hindering the access of positive particles The easiest path for the proton to enter the core will therefore be through one of its ends The fixed end is probably more or less an extension of the structure of the hair membrane At that end therefore the proton may be expected to pass rather freely *which means that there is electrical connection between* the core and the membrane of the hair and from there to the interior of the cell At the free end the situation may be different If the outermost unit of the threadlike molecule carries a carboxylate group the access for the proton into the core will be easy at that end as well In that case the molecule will act as an electric switch connecting the positive outside with the negative inside of the membrane of the hair The switch is on when the molecule is bent and off when it is straight We cannot however ignore the possibility that one or several of the outermost units of the molecule contain sulphonate groups (SO_3) instead of carboxylate groups If that is the case it will be more difficult for the protons to enter the core at its free end because the sulphonate ion in contrast to the carboxylate ion has very *little* if any tendency to take up a proton *it being an extremely weak base* Thus we may imagine two types of one sidedly fixed mucopolysaccharide molecules to exist Both of them create displacement potentials and take up a proton when they are

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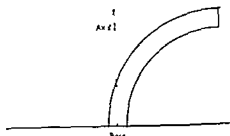


Fig. 1. A bent cylinder, a "handle", fixed to a base. When torsional forces are present inside the handle they will tend to turn it around the axis.

first edition appeared in 1863. This question has since been discussed in innumerable papers, which the present author is completely unable to collect and to discuss. As is well known, Helmholtz's theory is mainly based on two hypotheses: the hypothesis of the existence in the organ of Corti of a large number of resonators and the place hypothesis. The latter one is nowadays usually spoken of as the place theory and seems for good reasons to be generally accepted, while the former is still open to discussion.

In his fundamental work v. Bekesy has demonstrated (19) p. 403 that a sound wave impinging on the eardrum provokes travelling waves in the basilar membrane, and that the amplitudes of these waves have maxima in different distances from the stapes, depending on the frequency of the sound waves. Adopting the place theory we understand that the basilar membrane acts as a preliminary mechanical frequency analyser. According to the present picture the oscillations of the said membrane relative to membrana tectoria are transformed, through the action of bent hyaluronate molecules, into electrical currents which excite the nerve endings to emit action potentials into the nerve fibre in question. Evidently, however, the selectivity of the preliminary analyser is not by far sufficient to explain the surprisingly sharp pitch discriminating property of the human ear. v. Bekesy has further shown by direct experiments (20) that the feeling of a vibration is much sharper localised than one might expect from the extension of the vibrating area. Because of the close analogy between the sense of hearing and that of feeling which is so strongly emphasised by v. Bekesy, a similar effect will probably exist in the cochlea. This would result in a secondary sharpening of the primary analysis. But even so a still more refined tertiary analysis seems necessary. It seems to the present author that, following Helmholtz, we must believe that, to make the final analysis sufficiently selective, the organism must have resort to some kind of resonators.

It is from this point of view that we are now going to investigate whether the bent molecules acting as rotating motors may have a characteristic frequency of rotation. From the appendix, p. 46, it will be seen that it is actually possible to calculate a characteristic frequency (r) of rotation of the molecular motor. The calculation yields

and closings of "valves" for electricity But there is one important difference between the two mechanisms Davis assumes that the "valves" are operated by the bending of the *hairs* while according to the mechanism suggested here they are operated by the bending of hyaluronate *molecules* For bending the molecules through a right angle displacements of some tenths of a micron would suffice but to bend the hairs through an appreciable angle would require displacements many times larger than that This seems to speak strongly in favour of the molecular mechanism It may be added that the bending of the molecules must produce displacement potentials whose directions depend on the direction of the plane in which the bending takes place The potentials may therefore tend to modulate the current flowing into the cell in time with the wave motion in the basilar membrane

Forced Rotations of the Bent Hyaluronate Molecules Acting as Molecular Motors

We have assumed the molecules to be fixed with one end to the sensory hair We imagine the molecule to be roughly similar to a rubber tube glued at one end to a solid plane base Let us now bend the tube through a right angle as shown in Fig 1 the bent tube thus taking the form of a handle If this handle is turned once around an axis perpendicular to the base its free end will rotate once relative to the fixed one the axes of this rotation being in all positions parallel to the base If on the other hand there are torsional forces in the rubber tube they will force the handle to turn around the axis The question is now are there or are there not torsional forces in a bent hyaluronate molecule through which a current of protons is passing? Evidently if the protons move in the direction of the electrical force they will move in the bent molecule in directions which are everywhere parallel to its bent axis If that is the situation there cannot be torsional forces This however would require the straight molecule to have cylindrical symmetry But this is certainly not the case because the hyaluronate molecule is known to show optical rotation It may therefore be that the carboxylate groups and the other basic groups in the molecule are so arranged that to pass it from one end to the other a proton is compelled to move on a screw line Let us assume this to be the case In our rubber tube model the proton must then be compelled to move everywhere in a direction forming an oblique angle with the direction of the electric force Therefore on the above assumption there must arise torsional forces in the handle the bent molecule when the proton is drawn through it by the electric force In other words it is a consequence of our assumptions that supposing the molecule to be fixed as described on a sensory hair it will act when bent not only as an electric switch but also as an electric motor The energy necessary to turn the motor comes from chemical reactions in the sources of the two potential differences 80 mV and 60 mV mentioned before

The Question of Pitch Discrimination

The question of the understanding of pitch discrimination was raised by Helmholtz in his renowned book *Die Lehre von den Tonempfindungen* whose

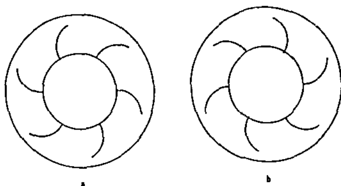


Fig 2 The innermost circles represent cross sections of a sensory hair seen from above It is arbitrarily provided with six molecules around its circumference The space between the two circles in Fig 2a or in Fig 2b represents the liquid or the jelly surrounding the hairs By an upward relative displacement of the hair at zero time the molecules are bent downwards Supposing the sense of rotation to be clockwise the situation after one fourth of a period will be as in Fig 2a and after three fourths of a period it will be as in Fig 2b

that this number is retained practically during the lifetime of the individual despite growth and wear of the molecules However it seems promising to investigate the consequences of the mechanism suggested

First of all we look into the consequences of resonance or non resonance between the vibrations of the basilar membrane and the supposed rotations of the molecules on the hairs

From v Bekesy s experiments (19) p 496 we know that the basilar membrane moves in relation to the tectorial membrane when the ear is exposed to sound waves The molecules on the hairs are therefore bent in time with the vibrations Whether the bending displacements of the surrounding substance liquid or jelly like are transversal or longitudinal relative to the hairs seems rather immaterial According to a drawing by v Bekesy (19) p 497 both kinds of displacements seem to result from the wave motion As however the longitudinal type is a little easier to describe than the other type is we shall restrict our discussion to that case

Fig 2 is intended to show schematically a cross section of a cylindrical *hair arbitrarily provided with six molecules evenly distributed on its circumference* The space between the two circles is supposed to represent the substance liquid or jelly like surrounding the hair Under the influence of the wave motion caused by the sound waves the two cylinders represented by the two circles must move in relation to each other because the innermost one is bound to follow the movements of the basilar membrane while the outermost one more or less follows the movements of the tectorial membrane Thus sound waves impinging on the eardrum will eventually produce shearing movements in the interspace between the two cylinders which must bend the molecules As described before the bending will cause the molecules to permit the passage of a current of protons and this current will compel the

$$\nu = 17 \times 10^9 / N^3 \text{ Hz} \qquad (2)$$

N is intended to mean the number of turns of the screw line on the cylinder representing the hyaluronate molecule and it is supposed to equal the number of units in that molecule

The specimens used for the measurements of displacement potentials were prepared from human navel cords According to molecular weight determinations the number of units in these molecules is about 1000 and this was used for the calculations of the potentials In other tissues however smaller molecular weights have been found In arterial walls for example Berthelsen & Marcker (21) found numbers about 100 For mucopolysaccharides isolated from the skin of mice Hvidberg & Jensen (16) found numbers ranging from about 650 to about 350 the number decreasing with increasing age It is therefore feasible to imagine that the molecules on the hairs of a certain cell are equal in size but that N varies from cell to cell If now on a certain cell $N = 1000$ we shall have for all molecular motors on that cell a rotational frequency of 17 Hz If on another cell the molecules are ten times shorter the rotational frequency for that cell becomes 17 000 Hz Evidently this range of frequencies corresponds rather closely to the range of sound frequencies audible to the human ear

The range in question covers about ten octaves Assuming 12 halftones on each octave this range the factor 1000 corresponds to about 120 halftones As the range from $N = 1000$ to $N = 100$ contains 900 integral numbers it might seem possible to understand the pitch discriminating property of the human ear simply by assuming that the sensory cells effective at hearing are divided in groups each group being characterised by the length of the hyaluronate molecules on their hairs One objection to this lies close at hand According to estimates in the literature 900 resonators are by far insufficient to explain the sharpness of the property in question The number should be multiplied at least with a factor of four This however does not prove that the picture disagrees with the experiments In this connection it should be remembered that according to the appendix the frequency is proportional to the potential difference across the wall of the hairs For a given length of the molecule the characteristic frequency of rotation may therefore be modulated by small changes of the potentials S H Mygind has reminded the author of the fact that the sensory cells in the organ of Corti are arranged in a matrix with a few columns and a great number of rows The total number of cells is certainly much larger than 900 Now nobody knows whether or not there are slight differences in the potentials of the cells e g those in the same rows of different columns If there are the number of different frequencies will most probably suffice to explain the extremely sharp pitch discriminating property of the ear On the whole the question of resonator capacity does not seem to be the worst difficulty for the picture To the present author a much more serious one is that one has to assume that the number of units in the molecules on each cell are precisely the same and

a pure tone of frequency $f = r$ After the sound has ceased the aforementioned energy sources still turn the molecular motors but now the balance between frictional loss and input of energy has been disturbed, the latter having been diminished by the energy of the sound waves Therefore, shortly after the sound has ceased the rotation of the motors will cease, the bent molecules will straighten, and the current will be switched off

If this picture is correct, cases may be expected where something has gone wrong with the structure of the molecular motors or with that of the membranes of the hairs, causing a never ceasing leaking in of electricity into the cell This would be felt by a patient as a never ceasing sound, probably as a nearly pure tone The author has been informed by an otologist that such symptoms actually occur, but of course he is well aware that the explanation is hypothetical to some extent

An Objection to the Theory

Broadly speaking the sketch of a mechanism for the excitation of the nerve endings seems to agree well with the experiments by v Békésy and with the experiments and views, which we owe to Hallowell Davis and his collaborators, as reported in his reviews (17 18) However, Galambos & Davis (23) and Tasaki (24) reported experiments in 1943 and 1954, respectively which seem to disprove, not only the hypothesis above, but any hypothesis which is based on resonance combined with the place theory Actually the two sets of experiments agree so well that we may restrict ourselves to discussing for example, Tasaki s results (24)

Tasaki exposed the ear of a guinea pig to pure tones of varied strength and pitch lasting for about 10–20 msec and investigated its effect on a single nerve fibre He then found that for weak sounds the nerve responded only to a rather narrow band of frequencies But for stronger sounds the frequency spectrum to which the nerve fibre responded was broadened, much to the deep side but rather little to the high side His results as well as those of Galambos and Davis seem to prove beyond doubt that a single sensory cell with its nerve fibre can be excited to emit action potentials by tones of widely different frequencies if the sound is strong At low intensities the behaviour of the cell seems to approach that predicted by any resonance theory combined with the place theory

With strong sounds however, the situation is different In the first place it may be mentioned that, quite apart from any theory, the experiments seem to imply that a deep pure, and strong tone must be heard as having a lighter timbre [illegible] also a direct consequence [illegible] understand how the ear fo[illegible] persons can have such a sharp pitch discriminating property as it actually has Such questions have been discussed by Davis (25) but the present author does not venture to touch on these physiological and psychical problems The physical phenomena observed by Tasaki are much easier to discuss As hinted at above, the worst difficulty is with the strong

molecules to rotate as described According to our hypothesis the characteristic frequencies of rotation of all the molecules on the same hair are equal, and the same must be true of their *sense of rotation* We may express this by saying that the molecules on a single hair form a coherent group

Thus, when all the molecules in the group are at a certain time in the same phase of rotation they will remain so for any length of time

Let us now assume the rotation to be clockwise Then, if the hair is displaced upwards, the molecules will become bent downwards and the bent molecules, the "handles", will begin to turn After the lapse of one-fourth *of a period the situation will be as in Fig 2a Then after three-fourths* of a period the situation is as in Fig 2*b* and so forth, if the handle continues to turn If, however, the frequency of revolutions of the handle (*r*) and that of the sound waves (*f*) are different, the frictional forces will soon stop the rotation, and the bent molecule will straighten out, at which the current through the molecule will be switched off In such a case the interior of the cell can only receive a small amount of electricity, which will suffice to start *at most one or a few action potentials* from the nerve ending

However, if the frequencies *r* and *f* are equal, the situation is quite different In that case the free end of the handle and the surrounding substance will both move upwards in Fig 2*a* and half a period later they will both be moving downwards The friction between the molecules and the liquid (or jelly) thus becomes much less in the case of resonance than it is in the non-resonance case There may even be a feed-back of energy from the electric sources *into mechanical energy of the substance surrounding the hair* Evidently, besides the effect of the molecular switch operating on the direct current from the exterior into the inside of the cell, there must be an effect caused by the displacement potential Because the bent molecules change their orientation in time with the wave motion in the basilar membrane, this potential must produce an alternating voltage containing the same frequencies in about the same proportions as those of the sound received by the ear Therefore, *it must be possible to demonstrate a microphonic* effect of the cochlea by means of suitably placed electrodes, As is well known, Wever & Bray demonstrated the existence of such an effect many years ago (22)

It is also known that v Békésy has demonstrated that the energy of the microphonic effect is essentially larger than that of the acoustic signal Professor Dohlman *has informed the present author that* in a conversation (1961) between him, D and v Békésy the latter estimated the energy of the microphonic effect to be about five times greater than the input of mechanical energy Evidently the present picture agrees, qualitatively, with this finding, the source of the excess energy being the chemical reactions which maintain the two often *mentioned potential differences in* the cochlea

Thus, in the case of resonance, a depolarising current will flow into the cell and this must give rise to the emission of a train of action potentials from the nerve-ending in question into its continuation as a nerve fibre The effect will continue so long as the sound impinges on the eardrum, the sound being

a pure tone of frequency $f = r$. After the sound has ceased the aforementioned energy sources still turn the molecular motors, but now the balance between frictional loss and input of energy has been disturbed, the latter having been diminished by the energy of the sound waves. Therefore, shortly after the sound has ceased the rotation of the motors will cease, the bent molecules will straighten, and the current will be switched off.

If this picture is correct, cases may be expected where something has gone wrong with the structure of the molecular motors or with that of the membranes of the hairs, causing a never ceasing leaking in of electricity into the cell. This would be felt by a patient as a never ceasing sound, probably as a nearly pure tone. The author has been informed by an otologist that such symptoms actually occur, but of course he is well aware that the explanation is hypothetical to some extent.

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With strong sounds, however, the situation is different. In the first place it may be mentioned that, quite apart from any theory, the experiments seem to imply that a deep, pure, and strong tone must be heard as having a lighter "timbre" than that to be expected from its frequency. It is also a direct consequence of the same experiments that it seems difficult to understand how the ear for some persons can have such a sharp pitch discriminating property as it actually has. Such questions have been discussed by Davis (25), but the present author does not venture to touch on these physiological and psychical problems. The physical phenomena observed by Tasaki are much easier to discuss. As hinted at above, the worst difficulty is with the strong

sounds, while weak pips (Tasaki's expression) seem to approach our expectations. Concerning strong pips, it must be remembered that movements of the basilar membrane must always bend at least some of the molecules on the hairs, and, if they are strong enough, they may bend so many molecules that enough electricity leaks into the cell *to depolarise it and therefore to* excite the nerve ending to emit action potentials, whether there is resonance or not. It seems therefore that only long lasting, and not too strong pure tones, are really suitable in testing the pitch discriminating property of the ear.

It should also be mentioned that it seems doubtful, from the standpoint of the theory of Fourier analysis, whether a sound of short duration, a pip, can ever be a pure tone. So far as can be seen, a pip whose main frequency is reasonably high must contain frequencies of the same order of magnitude as the reciprocal of the duration of the pip, that is, components of rather low frequency. Generally speaking, the shorter the duration of the sound is the more *ill defined is its frequency*. *The observation of Savart quoted by* v. Békésy in his Nobel Prize lecture (20), p. 206, that two cycles of a tone provide enough cue to determine the pitch of the tone, seems to be a challenge to any theory of pitch perception.

It thus seems that Tasaki's experiments can be understood on the basis of the mechanism suggested above, and that they do not, therefore, yield such strong arguments against its validity as one might believe at first sight.

The author extends his sincerest thanks to his friend Dr. Thure Vilstrup and to other colleagues mentioned above, for information, general advice and numerous discussions. Naturally, misunderstandings and errors are due to the author alone.

APPENDIX

Estimation of the Characteristic Frequency of Rotation of the Molecular Motor

Let us provisionally consider the conducting core of a hyaluronate molecule to be represented by a vertical straight cylinder of diameter $2a$, on whose surface a proton is bound to move on a screw line with N turns. Denoting the ratio of the height of one turn to the diameter by β, the height of the cylinder becomes $2Na\beta$. The slope $tg\mu$ of the screw line against the horizontal *plane is then defined by*

$$tg\,\mu = \beta/\pi \tag{3}$$

from which

$$\cos\mu = 1/\sqrt{1+\beta^2/\pi^2} \tag{4}$$

$$\sin\mu = \beta/\pi\sqrt{1+\beta^2/\pi^2} \tag{5}$$

If the potential difference between the ends of the cylinder is U, the potential gradient in the direction of the movement of the proton L becomes

$$L = U\sin\mu/2Na\beta \tag{6}$$

Let, furthermore, the molar conductivity of the proton in the molecule be λ. The linear velocity of movement of the proton v then becomes

$$v = E\lambda/F, \tag{7}$$

where F is Faraday's constant.

The number, s, of protons which pass a fixed point on the screw line in unit time must be the same as the number of protons which traverse one turn of the screw-line in unit time, and this must, at the same s, be the same as the number of turns passed by one proton in unit time. Now evidently

$$s = v\,d, \tag{8}$$

where d is the linear density of protons on the screw line. The length of the screw line is $2\pi a N/\cos\mu$ and there is one proton at a time in the screw. Consequently

$$d = \cos\mu/2\pi a N \tag{9}$$

From (7) and (8)

$$s = dE\lambda/F \tag{10}$$

We consider now the present case where the cylinder is bent through a right angle. In that case the lines of electrical force will be bent with the cylinder, while the length of the cylinder remains unchanged. The only difference from the case of the straight cylinder is thus that, while the angle μ in the latter case is constant, it oscillates between two different values in the case of the bent cylinder. If, however, N is large the difference between the two limiting values of μ will be small. The differences must, moreover, on an average nearly cancel each other. We therefore make only very small errors by using the same argument for the bent cylinder as we did for the straight one. (10) is therefore valid also for the bent cylinder, the "handle".

We shall now use the assumption that the movement of the revolving handle is periodic, but to prove its correctness is a complicated affair. We can only hint at the principle leading to this result. The proton must enter the first turn of the screw line on the bent cylinder at the place which is nearest to the centre of curvature of the bending. After having traversed the first turn it will again be at the place which is nearest to the centre of curvature and so forth, until it leaves the last turn at the place which is nearest to that centre. At that time the handle has made one revolution and the proton has traversed $N-1$ turns. That the number is $N-1$ and not N is due to the fact that the "places nearest to the centre of curvature" move on the *surface of the handle* during its revolution. Thus the proton traverses $N-1$ turns for each revolution of the handle. As N is a large number, we shall in the next equation replace $N-1$ by N.

As now s is the number of turns passed by the proton in unit time we get for the frequency (r) of rotation *of the handle*,

$$r = s/N = Ed\lambda/NF \tag{11}$$

Introduction of (6) and (9) in (11) and use of (4) and (5) yields

$$r = U\lambda/(4\pi^2 a^2 N^2(1+\beta^2/\pi^2)F) \tag{12}$$

Numerical estimate. β is probably not very different from unity. We therefore replace the factor $1+\beta^2/\pi^2$ by 1.1. For U we use 140 mV = 0.140 V. The molar conductivity λ of the proton *in the core of the molecule* is evidently unknown, but we may guess that it is not very different from the molar conductivity of protons in water, which is 315 Acm²/V mol. For a we take the value used in the calculation of

the displacement potential, 2.5×10^{-8} cm F is 9.65×10^4 A s/mol Using these values we get

$$\nu = 16.84 \times 10^9/N^2 \ s^{-1} = 16.84 \times 10^9/N^2 \ Hz, \tag{13}$$

which, evidently, because of the uncertainty in some of the values above, must be taken with a grain of salt

ZUSAMMENFASSUNG

Im Teil I wird die Bedeutung von Verschiebungspotentialen, verursacht durch Biegung von Hyaluronatmolekülen, für das Verständnis der elektrischen Phänomenen im Vestibularapparat diskutiert Es stellt sich heraus, dass die Schlussfolgerungen, die von der Existenz und von der Theorie der erwähnten Potentiale gezogen werden können, in Vorzeichen und Grossenordnung mit den von Lowenstein und Wersäll und von Trincker im Bogengangssystem beobachteten Erscheinungen übereinstimmen Vielleicht sind aber zwei etwas verschiedene Mechanismen, der eine ohne und der andere mit Verstärkung möglich *Im Teil II* wird versucht, ein Verständnis der für die Schnecke charakteristischen elektrischen Phänomene zu erreichen Insbesondere wird versucht, die nach Annahme periphersche Analyse von Schallen in bezug auf Tonhöhe zu erklären Der Hauptgesichtspunkt ist der von Helmholtz in 1863 angebahnte, dass die erwähnte Analyse durch irgendeine Art von Resonator Mechanismus, kombiniert mit der Annahme von Lokalisierung der Nervimpulse, erklärt werden muss Es besteht aber ein Unterschied zwischen der Annahme von Helmholtz und der hier vorgebrachten, insofern als Helmholtz Resonatoren vom Saitentypus sind, während hier angenommen wird, dass die Resonatoren durch molekulare Motoren mit definierter Rotationsfrequenz repräsentiert sind Es wird gezeigt, dass, wenn gewisse Bedingungen erfüllt sind, gebogene Hyaluronatmoleküle sowohl als „Ventile" für Elektrizität wie auch als rotierende Motoren mit definierter Umlauffrequenz wirken können Zum Schluss wird gezeigt, dass die Experimente von Galambos und Davis und von Tasaki nicht notwendigerweise der Richtigkeit des vorgeschlagenen Mechanismus widersprechen Eher will es scheinen als ob er die von den erwähnten Verfassern an einzelnen Nervenfibern beobachteten Erscheinungen mitführen muss

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Sundvaenget 9 Hellerup Denmark

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THE POSITION OF PARETIC VOCAL CORDS

K FAABORG-ANDERSEN
Nykobing F., Denmark

From the Departments of Oto-laryngology, The Finsen Institute (Head H Rasmussen, M D), Copenhagen and The Central Hospital (Head K Faaborg-Andersen, M.D), Nykobing F

Based on 883 cases of recurrent paralysis of which it was possible to re-examine the 346, the relation between the position of the paretic vocal cord and the clinical findings are discussed (Table 1) As the most plausible explanation of the fact that, in a small percentage of these cases the position of the paretic vocal cord and the clinical findings do not agree, partial denervation is mentioned

Immobility of one vocal cord can only be due to paresis of the recurrent nerve in the absence of such mechanical causes as tumor of the larynx, cicatrix in the larynx or anchylosis of the cricoarytenoid articulation

The following is at present the most generally accepted explanation of the different positions of the vocal cord in vocal cord paresis and is supported by the main body of recent work on this subject (Hofer & Jeschek, 1940, Negus, 1947, Murtagh & Campbell, 1952, Pressman & Kelemen, 1955, Faaborg Andersen, 1957)

If only the recurrent nerve is interrupted the vocal cord maintains a *fixed* paramedian position a few millimeters from the midline, since the crico thyroid muscle is unaffected If both the recurrent and the superior laryngeal nerves are interrupted, all the intrinsic laryngeal muscles are paralysed and the vocal cord assumes an immovable position in the intermediate position *between full adduction and full abduction, more lateral than the paramedian* position

Although this statement is generally accepted and in most cases in agreement with clinical findings, it is still possible to meet patients the position of whose paretic vocal cord is not in agreement with the clinical findings for example intermediate position caused by pressure of the nerve in the lower portion of the neck or the upper portion of the mediastinum

It was the aim of the study presented here to attempt to clarify this problem by re examination of several patients

AUTHOR'S INVESTIGATIONS

A review of records compiled over approximately the past 20 years by all oto laryngological departments in Copenhagen showed a total of 883 patients classified under the diagnosis of *recurrent paralysis* All these patients were

TABLE 1

Cause of paresis	No of cases	Total no of cases	No of cases re examined	No of cases not agreeing with clinical findings[a]
1 Postoperative				
A Operation for goitre		2 0	191	
B Other neck operations		20	3	
2 Compression				
A Malignant diseases (or lymph node involvements)		271		
(*a*) Carcinoma of the lung	86		0	8
(*b*) Carcinoma of the oesophagus	53		0	12
(*c*) Lymph node metastases	108		4	3
(*d*) Carcinoma of the thyroid gland	21		0	
B Other diseases		79		
(*a*) Aneurysm of the aorta	30		3	5
(*b*) Enlargement of the heart	20		2	3
(*c*) Goitre	29		21	
3 Diseases of the nervous system				
A Peripheral (neuritis)		93	93	
B Central		58	26	
4 Unknown (intraceable)		92	0	
		883	346	31

[a] Intermediate position No re-examination

requested to appear for re examination As expected most of them had died but the cause of the paralysis was clearly indicated in the great majority of records Only 346 appeared for re examination

Table 1 shows the cause of recurrent paralysis in these 883 cases

I have apart from the cause of the so called recurrent paralysis observed the position of the paretic vocal cords at first examination as well as at the re examination By doing so it is possible to decide whether the case is one of recurrent paralysis in which the vocal cord is in the paramedian position or one of combined paralysis of the recurrent and the superior laryngeal nerve in which the vocal cord is in the intermediate position Records are often somewhat incomplete and it has not always been indicated whether at the first examination the cord was *in central* paramedian or intermediate position

The position of the paretic vocal cord is shown in Tables 1 and 2 in which midline median and paramedian etc for the sake of clearness are described as paramedian while intermediate *cadaver lateral* and *abductal* positions are grouped under the description of intermediate position

TABLE 2 *The position of paretic vocal cords*

Operation for goitre 270 patients
Re examined 194 patients

Original position		Present position	
(1) Paramedian	141		
		Paramedian	*81*
		Receded	*60*
(2) Intermediate	15		
		Paramedian	5
		Receded	9
		Intermediate	1
(3) Not indicated	38		
		Paramedian	*29*
		Receded	8
		Intermediate	1

Group 1 shows that in 60 cases the paresis has receded at the re examination In Group 2 it is notable that in five cases the paresis has changed from intermediate to paramedian position This is in direct contradiction to the classic and now obsolete "Semon's law", according to which the vocal cord would at first be in the midline, the abductors being the first to be paralysed, and later change into intermediate position How is this to be explained? To begin with it must be borne in mind that, as the positions are described by two different examiners, the discrepancy may be due to their different interpretation of the paramedian and intermediate position respectively, if, however, the observations are correct, it follows that the vocal cord must have changed position Could this be due to contraction? I do not think so, but there may be another explanation As is evident from Table 2, Group 2, nine out of the 15 cases of paresis have recovered completely Is it not conceivable, then, that in the five cases where the position has changed from intermediate to paramedian the function of the superior laryngeal nerve has regenerated, while the recurrent nerve has remained paretic? This explanation appears to me the more probable

As shown in Table 1, I have succeeded in re examining 346 cases out of 883, the position of whose paretic vocal cord was in accordance with clinical findings Out of the remaining 537 cases, which I did not succeed in examining, the position of the paretic vocal cord was in 31 cases not in accordance with clinical findings

This is the experience of several other authors The majority of them do not attempt to explain the cause In recent years, however a few have tried to give an explanation Clerf (1953) found among 292 cases of recurrent paralysis many whose vocal cords were in intermediate position He explains this fact by referring to the extralaryngeal branching of the recurrent nerve described by several authors (King & Gregg, 1948, Morrison, 1952) It has been observed

that in 25 to 80 per cent of all cases division into two or more branches of the recurrent nerve occurs somewhere between the clavicula and the thyroid cartilage. Early division might cause lesion of the adductors, though not of the abductor branch, and this would result in an intermediate position.

This may be correct. I am not convinced though, as I do not believe that a lesion of the adductor branch would result in an immovable vocal cord. If there is function of the cricothyroid, arytenoid and posterior cricoarytenoid muscles the vocal cord will in my opinion be capable of movement, though not to the normal extent.

How frequently isolated lesion of the abductor or adductor branches actually occurs is difficult to say. Weddell, Feinstein & Pattle (1944) have described a case of "bilateral abductor paresis", presumably with immovable cords in the midline, in which isolated double denervation of the posterior cricoarytenoid muscles could be shown electromyographically, but this is the only case of isolated lesion of either abductor or adductor branches that I have been able to trace in literature. Personally, I have never, in spite of numerous investigations, found a single such case.

Jeschek (1953) found in 183 cases of recurrent paralysis five vocal cords in intermediate position, which could not be explained by the clinical findings. This he thought was due to retrograde degeneration of ganglia cells in nucleus ambigeus as shown by Hofer. Hofer has investigated the vagus nerve and nucleus ambigeus histologically in a number of these cases and found degeneration.

I am not convinced of the correctness of this explanation either. A retrograde degeneration of nerve fibres other than those injured and only in specially *selected cases*, appears to me a somewhat unphysiological explanation. Furthermore, this would supposedly result in complete paralysis of the vagus nerve on the injured side, and there is no question of *this*.

Zenker (1960) states after investigation of a very large *number of cadavers* that the size of glottis depends not only on the muscle *function*, *but also on* the individual quantity of fat and connective tissue in and around larynx. *He* is thus of the opinion that the vocal cord *in certain* cases may be in a rather more lateral than paramedian position, i.e. nearly in intermediate position, although *the case* is one of isolated paresis of the recurrent nerve. This may be correct. *I do not* know.

On the other hand, I am convinced that the position of the vocal cord is affected differently by partial and total *paresis*. In many cases of immovable vocal cord, it can be *demonstrated* electromyographically that there is only a partial paresis, as *several motory* units are still functioning, though fewer than normally. In fact, to *my mind* it is surprisingly seldom that abrogated electric activity or total denervation of the *intrinsic* larynx muscles are found in cases of immovable vocal cords.

I believe this may influence the position *of the* paretic vocal cord. If a certain number of motory units are still functioning, the muscles will have a certain tension, although they may not be able to contract actively. In the

majority of cases, this "tension distribution" will probably follow certain laws which will produce a characteristic position of the paretic vocal cord, but it is conceivable that the "tension distribution" between the different muscles, depending on the kind of lesion involved, in some cases might differ from the norm and thus affect the position of the paretic cord.

This, to my mind, is the most acceptable explanation of the fact that, in some cases, *though these represent only a small percentage of the total, the* position of the paretic vocal cord does not agree with clinical findings.

ZUSAMMENFASSUNG

Auf der Grundlage von *883* Fällen mit Recurrenslähmung, von welchen *316* Fälle nachuntersucht wurden, wird das Verhältnis zwischen der Stellung des gelähmten Stimmbandes und dem klinischen Fund besprochen. Als die wahrscheinlichste Erklärung darauf, dass man bei wenigen Prozenten der Patienten keine Übereinstimmung zwischen der Stellung des gelähmten Stimmbandes und dem klinischen Fund findet, wird die *partielle Denervierung genannt.*

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E N T Department, The Central Hospital,
Nykobing F, Denmark

Received April 2, 1963

GELLÉ TEST WITH BÉKÉSY AUDIOMETRY

III Findings with Salpingitis

GODFREY E ARNOLD and PETER SCHINDLER
New York N Y, U S A

From the Department of Research New York Eye and Ear Infirmary

After describing the technique of performing the Gellé test with Békésy audiometry, and following the definition of the range of normal values this paper is devoted to the findings in cases of salpingitis It could be confirmed that negative intratympanic pressure is counteracted by negative meatal pressure At that moment, the hearing loss resulting from tubal obstruction is temporarily corrected

It appears that negative pressure application during the Gellé test closes the air bone gap of salpingitis momentarily For this reason, the normal threshold shift, observed with negative meatal pressure, is inverted to an improved hearing level Three patterns of Gelle test results are discussed, which seem to reflect the degree of tubal obstruction

Borderline Cases

After having gained sufficient experience with the correct procedure of performing the Gelle test (Arnold & Schindler 1963*a*) we felt ready to define the range of normal reactions in healthy young adults Similar to the considerable scattering of normal behavior around an average midpoint obtained in other psycho acoustic experiments or with vestibular testing the normal reactions to the Gelle test extend over a rather wide range These individual variations of the temporary threshold *shift* (TTS) in response to altered meatal air pressure have been discussed in a second paper (Arnold & Schindler 1963*b*)

When beginning to evaluate our *records obtained* in normal cases we were amazed at certain exceptional phenomena They did not seem to fit into the regular pattern which prevailed in most normal young adults For example when testing our new young *residents* we came across the following peculiar case A young man without history of previous ear disease and with subjectively normal hearing produced the Bekesy tracing shown in the upper portion of Fig 1 The three closely adjacent curves represent his pure tone threshold obtained by recording first with rising frequency, then backward with falling frequency, and once more up with rising frequency There can be no doubt that his threshold for the low tones between

This study was aided by the John A Hartford Foundation of New York

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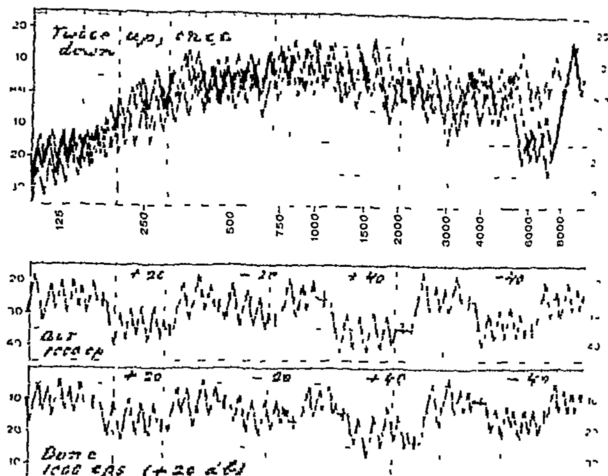


Fig. 1. Upper portion: Békésy recording in a subjectively normal young person afflicted by slight tubal obstruction. Lower portion: Gellé test by AC and BC at 1000 cps, showing inverted effect of negative pressure which is less effective than in normal cases.

about 100 and 300 cps is significantly poorer than that of many other young normal persons (comp. Fig. 2 in the first paper (Arnold & Schindler 1963a) and Fig. 1 in the second paper (Arnold & Schindler 1963b)).

During the subsequent Gellé test, the findings appeared puzzling at first glance. The second curve in Fig. 1 represents the air conduction (AC) response to altered meatal pressure in this subject. At 1000 cps, positive meatal pressure of 20 cm H_2O produced a TTS of only about 8 db. Although negative pressure is normally more effective than equivalent positive pressure, −20 cm H_2O resulted in a TTS of only 4 db. Likewise, +40 cm H_2O led to a TTS of 10–11 db, whereas −40 cm H_2O shifted the threshold by 7–9 db. The subject stated that he could not endure the pressures of ±50 cm H_2O because he felt pain. Most of the other test subjects encountered no such difficulty.

Exactly the same observation was made in the bone conduction (BC) curve at 1000 cps shown in the lowermost curve of Fig. 1. Again the amount of TTS in response to altered meatal pressure was much smaller than is normal. And again the negative pressures were less effective than the posi-

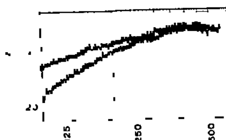


Fig 2 Threshold recording of a normal person after producing artificial retraction of the drum membrane (lower curve) and following tubal inflation (upper curve)

tive counterparts This reversal of the pressure relationships or the inverted effect of negative air pressure in the ear canal appeared to be typical of this case

The explanation came when we reexamined the ears of this person His ear drums appeared slightly retracted the tubes could not be inflated easily by catheter he was not able to inflate them spontaneously by the Valsalva maneuvre and he admitted to feeling a sensation of clogged ears when descending with an express elevator He had a slight condition of tubal obstruction which accounted for all his subnormal findings the slight low tone loss as well as the abnormal behavior of his Gelle test curves

Curious to find out whether a minimal transitory change of intratympanic air pressure could produce a measurable TTS we performed the following experiment Subject A whose test results were discussed in the first paper (Arnold & Schindler 1963*a*) closed his nostrils and swallowed at the moment the door of the test room was slammed shut Owing to the airtight seal of the door its closing causes a slight and brief increase of air pressure within the cabin The tested individuals usually swallow or perform the Valsalva maneuvre to reestablish normal intratympanic pressure As stated subject A did the opposite he swallowed with closed nostrils which aspirates air from the middle ear through a patent tube Thus the increased external pressure and the decreased intratympanic pressure were superimposed producing retraction of the ear drums A slight sensation of clogged ears was felt but the urge to swallow was suppressed while a threshold tracing was recorded with slow speed

The result is seen in Fig 2 lower curve Subsequently the subject inflated his tubes until the ears felt open and a second threshold tracing was recorded the upper curve in Fig 2 It can indeed be seen that negative pressure behind the ear drum caused a slight TTS of 10 db at 100 cps which decreased progressively with rising frequency From 250 cps on the two recordings are virtually identical This is not to imply that these higher frequencies are not depressed by negative intratympanic pressure Our recording indicates merely that this subject was unable to maintain the artificial

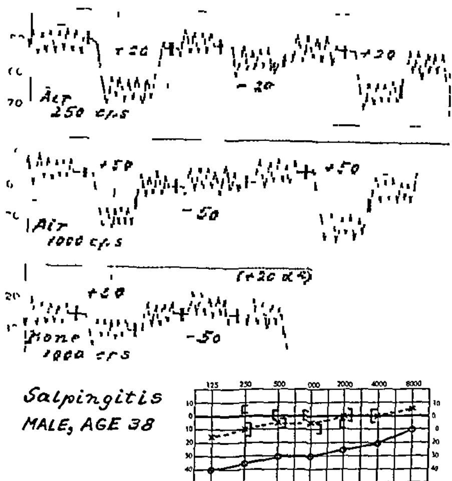


Fig 3 Inverted effect of positive and negative meatal pressure in a case of unilateral salpingitis negative pressure being of little effect on the threshold by AC and BC

negative pressure in his middle ear Even though he tried not to swallow his patent tubes admitted enough air to the middle ear so that normal pressure was established after about one minute the time it took to record from 100 to 250 cps

The Effect of Tubal Obstruction

As is well known from numerous previous studies which were discussed in the first paper (Arnold & Schindler 1963*a*) negative pressure within the middle ear counteracts the threshold shifting effect of negative air pressure in the external canal In fact when the two negative pressures become equal the pure tone threshold reaches its optimum It is thus possible to measure the value of negative middle ear pressure by reading the pneumophone value at the point of optimal hearing This was the original application of Van Dishoeck s pneumophone method

Studying our cases of salpingitis serous otitis and adhesive otitis, all with the clinical sign of ear drum retraction, we came across some interesting findings It could indeed be confirmed that tubal obstruction ...

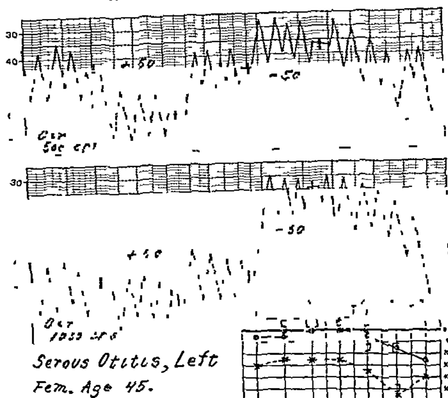


Fig 4 Slight effect of positive pressure on AC (at 500 and 1000 cps) while negative pressure closed the air bone gap in a case of unilateral serous otitis Note threshold improving effect of negative pressure for a short while

with characteristic changes in the Gelle test results Fig 3 illustrates a case of unilateral salpingitis in a man of age 38 as shown in his audiogram Testing at 250 cps the affected ear experienced a TTS of about 15 db when positive pressure of +20 cm H_2O was applied twice In characteristic contrast negative pressure of 20 cm H_2O resulted in a TTS of only 5 db (uppermost curve) When pressures of +50 cm H_2O were applied twice at 1000 cps a marked drop of the threshold occurred again Negative pressure of 50 cm H_2O however had no effect on AC at this frequency *The BC* findings are equally convincing Tested at 1000 cps positive pressure depressed the threshold tracing slightly (by 5 db) whereas negative pressure *elevated* the threshold curve by 3–4 db These findings were corroborated by tubal inflation it improved the patient s hearing and was followed by a normal result of the Gelle test Likewise his Gelle test of the *normal* left ear produced normal results What we see here is an inverted effect of positive and negative values the latter no longer being more effective

One of the most impressive and flawless recordings obtained among some 20 patients suffering from tubal obstruction is shown *in Fig 4* A woman of

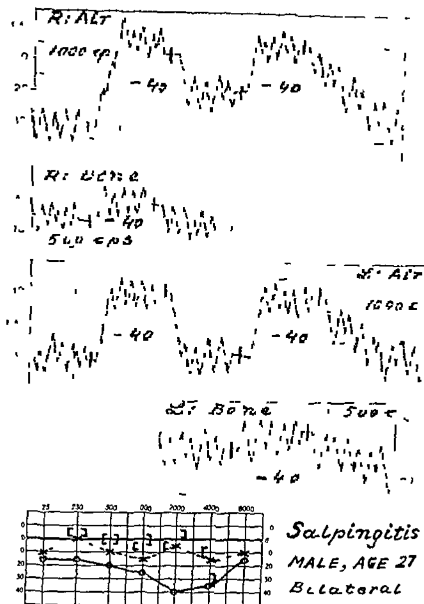


Fig. 5. In a case of bilateral salpingitis, the air-bone gap was temporarily closed by application of negative meatal pressure. In contrast to the normal result, negative pressure improves the threshold, AC being more affected than BC.

age 45 had an attack of serous otitis in the left ear. The other ear was normal except for slight premature presbycusis. Even though this person produced rather large excursions of the spikes, ranging between 10 and 20 db, her reaction to the altered pressures was very prompt and accurate. At 500 cps by AC, positive pressure of +50 cm H_2O depressed the threshold curve by about 16 db. In contrast, the equivalent negative pressure elevated the threshold by 10 db to the normal value.

It is interesting to note that the subsequent threshold recordings with normal pressure remained at first at the improved level until the spikes descended gradually to the original level. This observation may be inter-

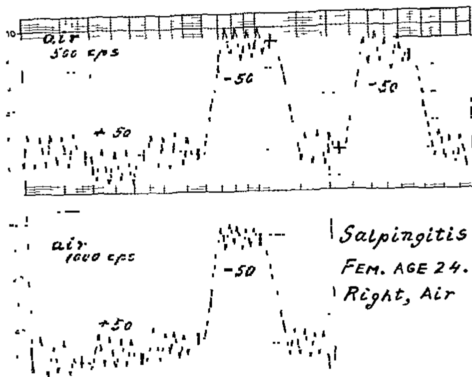


Fig 6 Extreme response to negative pressure in a case of salpingitis, showing almost complete absence of TTS with positive meatal pressure by AC at two frequencies

preted in the following manner Since the negative meatal pressure equalizes temporarily the negative middle ear pressure, it draws the retracted drum outward to a more normal position In principle, this mechanism is similar to the beneficial effects of tubal inflation It seems as if the negative meatal pressure had acted like slight tubal inflation, but the improvement did not last long Several other patients showed the same phenomenon of improved threshold following negative pressure application The same observations were made at 1000 cps by AC, again with short improvement of threshold after negative pressure This patient's normal ear produced a normal Gellé test

Fig 5 demonstrates a complete record in a case of bilateral salpingitis (male, age 27) In the more affected right ear, the negative pressure test, applied twice at 1000 cps by AC, caused marked improvement of the threshold Again, it was followed by brief improvement of hearing, as expressed by the downward slope of the non pressured threshold recording It is characteristic that the threshold decrease with negative pressure is less marked by BC than with AC Precisely the same findings were obtained from the patient's less afflicted left ear When the db values of the TTS are

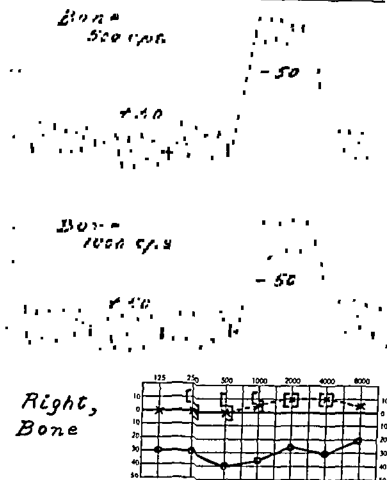


Fig. 7. Marked response by BC to negative pressure in a case of unilateral salpingitis, improving the BC threshold to the same degree as AC.

compared with the air bone gap shown in the audiogram, perfect agreement of the readings is seen. In other words, negative pressure closes the air–bone gap of tubal obstruction for the duration of the test.

A peculiar record is shown in Fig. 6. A young girl suffering from unilateral salpingitis showed a very slight depression of the +50 cm value at 500 cps by AC (6 db). Her response to −50 cm H_2O however, was extreme, shifting the threshold by 35–40 db, the amount of her air–bone gap. A repeat test with −50 cm H_2O at 500 cps confirmed the reading within 5 db. The same observations were made at 1000 cps by AC, again with closure of the air–bone gap at −50 cm H_2O pressure.

While these reactions with AC testing can be understood, it is less clear why this patient's *BC record* (Fig. 7) *should follow the same pattern*. As seen in the audiogram, BC is elevated to the absolute value. Even so, it is not clear why negative pressure, both at 500 and 1000 cps, should elevate the BC reading to such an extent. As explained in the first paper (Arnold & Schindler, 1963*a*), the BC recordings obtained by connecting a Beltone BC

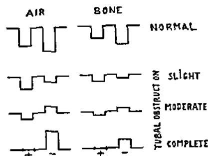


Fig 8 In contrast to the normal reaction salping tis seems to cause three types of an abnormal Gellé test reflect ng the degrees of sl ght moderate and complete t ibal obstruction

receiver to the Békesy audiometer represent purely relative values because they are not calibrated to the zero line Hence it is possible that such relative values may permit a major TTS to lower db values This problem deserves further study

CONCLUSION

After having studied additional cases of tubal obstruction the following patterns seemed to emerge Recalling what was said in the first paper (Arnold & Schindler 1963*a*) on the behavior of normal persons when subjected to the Gelle test the normal test result may be summarized as follows Fig 8 shows a graphic definition of the normal Gelle test in the upper row Positive pressure is less effective than negative pressure Likewise BC is less affected than AC

Completely different patterns are found with tubal obstruction In the lower section of Fig 8 three patterns are defined graphically It appears at the present stage of our experience that slight obstruction reduces the amount of TTS with positive pressure and inverts the ratio of effectiveness between the two types of pressure negative pressure becoming less effective Fig 1 is an example of this type

Moderate tubal obstruction appears to be characterized by the following pattern While positive pressure depresses the threshold curve only slightly (to higher db values) negative pressure elevates it moderately (to lower db values) in reference to the original reading The case described in Fig 4 is a good example of this type

It seems to be typical of severe or complete obstruction that positive pressure becomes ineffective whereas negative pressure *produces* a marked improvement of the threshold closing the air–bone gap Fig 6 and 7 illustrate an example In each case BC follows the pattern of AC even though to a lesser degree which is normal

Summarizing these preliminary impressions they may be condensed

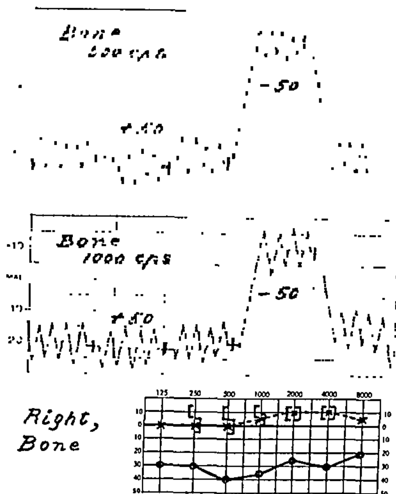


FIG 7 Marked response by BC to negative pressure in a case of unilateral salpingitis, improving the BC threshold to the same degree as AC

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ULTRASTRUCTURAL ORGANIZATION OF THE EPITHELIAL LINING IN THE ENDOLYMPHATIC DUCT AND SAC IN THE GUINEA PIG

P G Lundquist R Kimura[1] and J Wersäll
Stockholm Sweden

From the Department of Otolaryngology (Head Prof C A Hamberger) Karolinska Sjukhuset and King Gustaf V Research Institute (Head Prof G Birke) and the Department of Histology (Head Prof N Å Hillarp) Karolinska Institutet, Stockholm 60

The finer details of the epithelial lining of the endolymphatic duct and the proximal intermediate and distal portions of the endolymphatic sac have been described The most highly differentiated and active part of the entire areas was the intermediate portion where pinocytosis appeared to be a main function These active cells demonstrated numerous microvilli pedicels concentration of mitochondria many short endoplasmic reticuli and a rich vacuolar system The infolding of the cytoplasmic membrane was noted near the base of the cell and particularly between adjacent cells A rich network of the capillaries with fenestrated endothelium was observed in relation to the basement membrane of the sac proper The epithelial organization and vascularization of this area seemed to be ideally suited for passing fluid from the lumen towards the loose connective tissue

INTRODUCTION

In recent years considerable interest has been taken in the mode of circulation of the endolymph in the inner ear The histopathological demonstration of hydrops and alteration in the chemical composition of the cochlear fluid have been reported in connection with the Meniere s disease It has generally been regarded that the endolymph of the cochlear system is produced by the stria vascularis and that of the vestibular system by *the planum* semilunatum The absorption of the endolymph is said to take place locally within the two different systems as well as in the endolymphatic sac The anatomical orientation and the cellular morphology of the endolymphatic duct and sac have been previously described by Boettcher (1869) Portmann (1919) Guild (1927) Siirala (1942) Secretan (1944) Saxen (1951) and others

A detailed study of the endolymphatic sac of the guinea pig by Guild (1927) attempts to relate structure to function He states that the intermediate portion of the sac is concerned with the active *absorption of* endolymph and it is neither a vestigial structure nor a source of endolymphatic secretion While his view is shared by a few investigators the obliteration of the endolymphatic

[1] Harvard Medical School and Mass Eye and Ear Infirmary Boston U S A

into the following formula There are numerous transitions between these chief types found in clinical practice

Normal: positive pressure less effective than negative pressure, AC more affected than BC

Tubal obstruction: AC remains more affected than BC (1) slight pos slightly reduced, neg more reduced, (2) moderate pos greatly reduced, neg slightly inverted, (3) complete, pos ineffective, neg completely inverted

ACKNOWLEDGMENT

Gratitude is expressed to Mrs Yolan Schuller, Research Technician, for her meticulous test recordings and subsequent numerical evaluations, also to all volunteers who served as normal control subjects

ZUSAMMENFASSUNG

In zwei früheren Arbeiten wurden die Technik des Gellé-Tests mittels Békésy-Audiometrie sowie die Definition der normalen Grenzwerte beschrieben Die vorliegende Studie befasst sich mit den Befunden im Falle von Tubenverschluss Es konnte bestätigt werden, dass negativer Luftdruck im Mittelohr durch negativen Druck im äusseren Gehörgang ausgleichbar ist In diesem Augenblick ist der auf Tubenverschluss beruhende Hörverlust kurzfristig aufgehoben

Es scheint demnach, dass negative Druckeinwirkung während des Gellé-Versuches die Luft-Knochen-Distanz (air-bone gap) vorübergehend ausgleicht Aus diesem Grunde ist der normale Hörverlust, welcher in gesunden Ohren während der negativen Druckeinwirkung auftritt, in eine verbesserte Hörschwelle umgekehrt Drei Typen eines abnormen Gellé Test Resultates scheinen den Grad eines Tubenverschlusses anzugeben

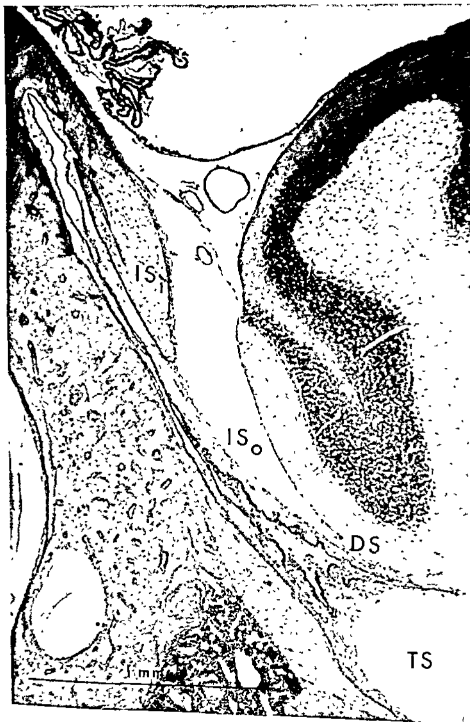
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Division of Otolaryngology U of Mississippi Medical Center, Jackson 6 Miss U S A

Received March 8, 1963


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sac in the cat (Lindsay, Schuknecht, Neff & Kimura 1952) has not resulted in any apparent histological changes in the inner ear or significant alteration in auditory acuity. Experimental evidence (Altmann & Waltner 1950) indicates that cochlear fluid is absorbed at other sites as well as the endolymphatic sac. Whatsoever its physiological importance may be, however, finer details of the epithelial lining of the sac is lacking. In this study, the electron microscopic cytology is clearly drawn and a possible function discussed.

MATERIAL AND METHODS

Six young healthy guinea pigs weighing 250 to 350 grams were used for this investigation. After decapitation the brain and cranial nerves were carefully dissected out from the skull without disturbing the endolymphatic sac and its adherence to the transverse sinus. The fixative (1 % buffered osmium tetroxide) was placed into the cistern of the vestibule within the first five minutes after death, the stapes having been previously removed and its peripheral area widened. In a few specimens, in order to facilitate fixation, a direct incision was made transversely into the endolymphatic sac at the cranial aperture of the vestibular aqueduct. The dissection was accomplished in 70 % alcohol with a very fine knife, the dura, transverse sinus, intermediate and distal portions of the sac remaining intact. The proximal and intermediate portions within the vestibular aqueduct were visualized after removing the bony wall on the medial side. They were gently removed from the bone in one piece using a fine flat knife. The endolymphatic duct, including bony fragments, was then dissected out from the vestibular side with an extra fine dissection needle. For the convenience of localizing the different areas in a few specimens each piece of the duct, proximal, intermediate and distal portions were processed separately. The specimens were imbedded in Epon and photographed with an Elmiscope I at the initial magnification of ×1000 to ×40 000.

RESULTS

The examination of the endolymphatic duct and four different areas of the sac, namely proximal, intermediate portions both within and without the vestibular aqueduct, and distal portion, indicated that there was a greater difference between the cell types of the duct and sac than within the sac proper. The size and shape of the epithelium in the sac varied considerably depending on age of the animal and also on the stage of cellular activity. For the convenience of descriptive purposes, the nomenclature proposed by Guild is extremely useful and is adopted throughout this paper (Fig. 1).

Fig. 1. Low power light microscopic view of the endolymphatic duct (ED) and the four different parts of the sac. Proximal portion (PS) gradually widening into the first part of intermediate portion (IS_i) completely covered by bone, followed by the second part of intermediate portion (IS_o) which is the most active and complex part outside the vestibular aqueduct close to the transverse sinus (TS). In the extreme end the sac flattens into the distal portion (DS). Hellent ahn Susa. C7.



F G 3 The prox mal port on The cel s are ve y s milar to those of the duct bu they ha e more m o ll at the cell su fa e The c topla m conta ns more nclu ons and vacuo es Osm um



FIG 2 The low cuboidal epithelium of the endolymphatic duct with an irregular nucleus, small dense cytoplasm with evenly distributed mitochondria and very few microvilli at the fluid surface. Osmium tetroxide × 30,000



I G 4 Intermed ate port on with h gh cubo dal and columnar cell The nucleus is round and the c topla n ncludes numerous m tochondria and vacuoles Cell borders are irregular with pronoun ed info d ng of the cytoplas n n the basal parts (nsert) Note legenerating cell mass in the lumen of the sac Osm um tetrox d 6 00 and 13 000 (n ert)

scattere l short en l plasmic tubuli Palade granules membrane formation l el nging to the Golgi apparatus large inclusion l odies and dark oval formations The apical cell surface was provi led with numerous microvilli an l cluf like projections whilst at the l ase the l asement meml rane was extremely irregular (I igs 5 ( ) Many f nger like projections of the cell walls

The Endolymphatic Duct

The epithelium was of a simple squamous or cuboidal type (Fig 2) The nucleus occupied a large portion of the cytoplasm with one or more deep invaginations The chromatine was condensed at the invaginations and the nuclear membrane The cytoplasm contained scattered oval shaped mitochondria, short endoplasmic reticulum, Golgi like structures, and occasional inclusion bodies The surface on the apical side of the cell was convex with a few microvilli, and on the basal area it was lined with a comparatively smooth basement membrane The cell wall between the adjacent cells showed some finger-like projections The subepithelial connective tissue was rather loose, filled with fluid and fine fibrous structure The capillaries were not many and located some distance from the epithelial lining The endothelium of the capillary did not show any apparent specialization in the present investigation

The Endolymphatic Sac—the Proximal Portion

This area was shaped in form of a triangle or an arrow head, and was covered with duct-like cells (Fig 3) and with cells similar to the high cuboidal type of the intermediate portion The nucleus was oval with a few invaginations, and was more often located close to the apical portion of the cell The cytoplasm contained scattered oval or rod-shaped mitochondria, endoplasmic reticulum, Golgi apparatus and a varying number of large dark bodies More vacuoles began to show throughout the cytoplasm The cell surface demonstrated an increasing number of microvilli on the apical zone, and there was more waviness on the basement membrane The cell wall between the adjacent cells showed loose finger like interdigitation In the connective tissue fibroblasts were found, with numerous irregular cytoplasmic extensions and capillaries in which the endothelium often contained very fine membranous fenestrae

The Intermediate Portion

There were many crypts in the epithelial lining with a considerable variation in size and shape of the cells ranging from cuboidal to columnar type Some cells were degenerated and were released into the lumen of the sac (Fig 4) The nucleus was oval or elongated, and its location was variable The nuclear membrane was formed of two separate layers, the outer one opened towards the cytoplasm and communicated with numerous vacuoles The cytoplasm contained a great number of elongated mitochondria, many aggregated close to the apical surface and a few at the base of the cell Some of the mitochondria were degenerating into either dark masses with distinct outer membranes or into extremely swollen 'balloons' There were a remarkably large number of small and large vacuoles, often interconnected to each other with a slight tendency to accumulate at the apical zones The cytoplasm was rich in



Fig. 6 Club like protrusions from upper cell border of a cell from the intermediate portion Note dense ribosomes in the protrusions and three layered plasma membrane Osmium tetroxide 8,000



Fig. (a) Top surface of cell from ... late portion ... protruding ... for protrusions and pinocytotic vessicle. (b) Bottom part of cell from ... area. Note the ... folding of the plasma ... membrane ... basement membrane. Osmium tetroxide ... (top) and ×16 000 (bottom).



Fig. 8. Light and dark cells from a crypt in the intermediate portion of the endolymphatic sac. The dark cells with more irregular nuclei with invaginations and a more dense cytoplasm with a less number of microvilli. Osmium tetroxide. × 4000.

showed irregular thicknesses and protrusions into the lumen. Pores were seen in the capillary wall covered by only a fine membrane. The diameter of the pores was around 450 Å (Fig. 7). There were no nerve elements demonstrable near the epithelium in the present investigation.

In the epithelial lining cells with light and dark cytoplasm were found intermixed at random (Fig. 8). They were identical in size and shape, however the dark ones often contained a less number of microvilli, irregular nucleus with invaginations and cytoplasm with reduced number of mitochondria and dark ground substance.

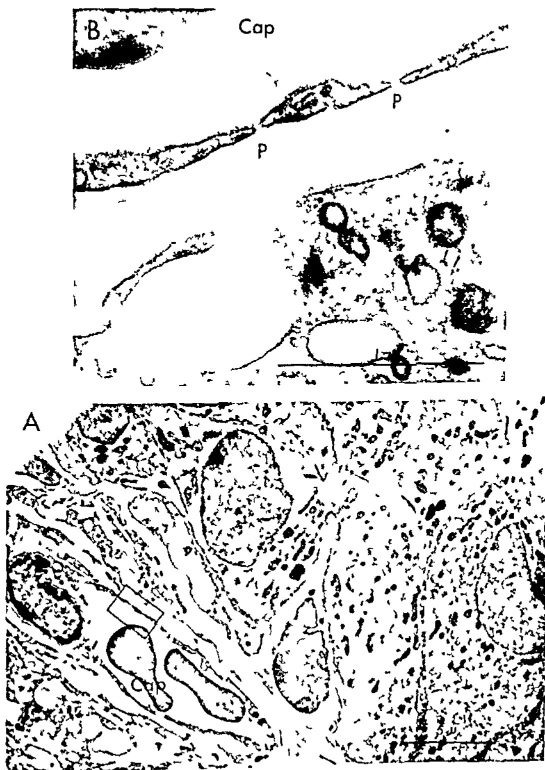


Fig. 7 (a) Capillary (Cap) in intermediate portion located close to the basal part of the epithelial cells with frame showing margins of the endothelial wall which in higher magnification (b) shows pores (P). Osmium tetroxide ×4300 (a) and ×47 000 (b)

were located below the terminal bars, particularly near the base, without extending much towards the cytoplasm. In the connective tissue there was a rich capillary network located close to the base of the epithelium. The endothelium of the capillaries was limited by a fine basement memb nd

The general cytological characteristics were similar to the intermediate portion though with less complexity. The number of the microvilli, mitochondria, membranous structures, vacuoles and inclusion bodies were reduced. At the proximity of the basement membrane were numerous capillaries with fenestrae similar to those described in the intermediate portion.

DISCUSSION

The present investigation confirmed the extreme accuracy of Guild's description of the endolymphatic duct and sac, particularly in regard to the cellular outline and subdivisions of the sac proper. Based on our morphological findings the intermediate portion of the sac appeared to be the most highly differentiated and active part of the entire epithelial lining. There were, however, some differences in the degree of cellular activity in each of these zones depending perhaps on the condition and age of the labyrinth. For example in a spot check of the intermediate portion of an endolymphatic sac taken from a large elderly guinea pig, vacuoles and dark inclusion bodies were more pronounced than in a similar specimen taken from a young guinea pig (Fig. 10). The cells of the intermediate portion were of two types, one with light and one with dark cytoplasm representing different stages of metabolic activity, the latter being the more mature. Occasionally these cells were shed into the fluid space and "the free floating cells in the lumen" (Guild 1927) were in part at least composed of these.

The experiments of Guild (1927) and Andersen (1948), who injected various dyes into the labyrinth and other areas of the inner ear, indicated that the concentration of these substances was highest in the epithelium of the intermediate portion. Our investigation revealed that these cells of the intermediate area were engaged in great pinocytotic activity and were provided with numerous microvilli, pedicles, extremely rich vacuolar system, many mitochondria, membranous structures and large inclusion bodies. We have also seen in a number of cases these cells having the ability to take up fairly large solid particles into their cytoplasm (cf Engstrom & Hjort 1950).

It has been reported that the cells which specialize in fluid transport or in secretion show pronounced infolding of the plasma membrane so as to increase the surface area, as demonstrated in the kidney (Sjostrand & Rhodin 1953, Pease 1955), in the ciliary body of the eye and of the submaxillary gland (Pease 1956) and in the pancreas (Ekholm *et al* 1962). The infolding of the plasma membrane in our material was more pronounced between adjacent cells near the base (Figs. 4, 5) in a somewhat similar manner as described in the choroid plexus (Maxwell & Pease 1956). Such interdigitation would increase the border surface between two cells and thus enhance the capacity of fluid transport between them. From the morphological standpoint therefore it would appear that the endolymph would pass more easily through the cells than through the terminal bars and the few desmosomes between the cells. The present investigation showed that the basement membrane was



FIG 9 High cuboidal epithelium from the distal part of the endolymphatic sac showing the more smooth arrangement of the epithelium with less number of microvilli and fewer inclusions in the cytoplasm At the proximity of the basal membrane a capillary with pores is found (arrows) Osmium tetroxide × 6800

The Distal Portion

Cuboidal and low cylindrical epithelial cells were found in this area (*Fig. 9*). Some of them looked somewhat similar to the duct cells. The epithelial lining was much smoother and the cells were arranged in a more orderly fashion.

The general cytological characteristics were similar to the intermediate portion though with less complexity. The number of the microvilli, mitochondria, membranous structures, vacuoles and inclusion bodies were reduced. At the proximity of the basement membrane were numerous capillaries with fenestrae similar to those described in the intermediate portion.

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FIG 10 Section from intermediate portion of the endolymphatic sac of a normal, old guinea pig showing numerous pigment like inclusions and vacuoles in the cytoplasm The darker cell is apparently in a process of degeneration (*Dc*) Osmium tetroxide × 12,000

present as a continuous structure throughout both duct and sac as opposed to the earlier findings of Guild where although the complex nature of the basal part of the cell was appreciated he was unable to note the basal membrane

Pores in the endothelium of the capillary were well demonstrated particularly in the intermediate and distal areas of the endolymphatic sac (Fig 7) Such pores or fenestrae were covered by a thin membrane, described by Rhodin (1962) in the kidney tubules and were present in cells concerned with fluid transport The fenestrae may be regarded as a special feature of this type of cell

We were unable to find any specific and consistent activity which could be regarded as indicating secretory activity of the epithelial lining However we could not altogether rule out that possibility as we occasionally observed clear globules on the apical surface of the cells in the intermediate portion Whether these globules were due to the fixation degeneration mechanical trauma or were in fact cellular secretions was not clear

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ZUSAMMENFASSUNG

Die feineren Details von dem Epithel des endolymphatischen Ganges und von den proximalen intermediären und distalen Teilen des endolymphatischen Sackes sind beschrieben worden Der differenzierteste und wirksamste Teil war der intermediäre Abschnitt wo Pinocytosis eine hauptsächliche Funktion zu sein schien Diese aktiven Zellen wiesen plasmatische Reticuli und ein reiches Vacuolensystem auf

Die Faltenlegung der cytoplasmatischen Membrane wurde an der Base der Zelle und besonders zwischen nachbarlichen Zellen unterschieden

Ein reiches Netzwerk von Kapillaren mit fenestriertem Endothelium wurde beobachtet ausschliesslich auf der Basalmembrane des eigentlichen Sackes

Die Organisation des Epithels und die Vascularisierung dieses Abschnittes schienen dem Transport von Flüssigkeit von dem Lumen zu dem zarten Bindegewebe ideal angepasst zu sein

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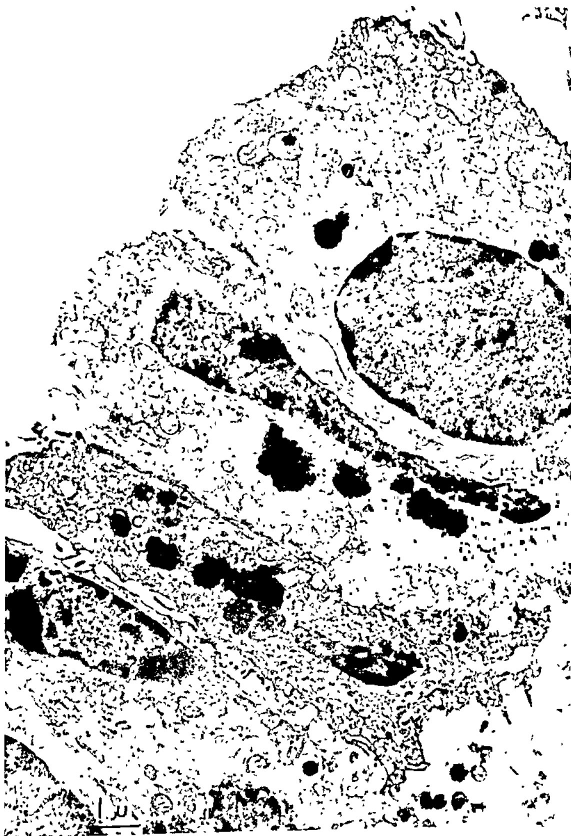


FIG. 10. Section from intermediate portion of the endolymphatic sac of a normal, old guinea pig showing numerous pigment like inclusions and vacuoles in the cytoplasm. The darker cell is apparently in a process of degeneration (*Dc*). Osmium tetroxide. × 12,000

HABITUATION, EFFERENCE AND VESTIBULAR INTERPLAY

III. Unidirectional rotatory habituation

E. Fluur and I. Mendel
Stockholm, Sweden

From the Department of Otolaryngology (Head: Prof. C. A. Hamberger, M.D.), Karolinska sjukhuset, Stockholm 60

Fourteen vestibularly normal human subjects were subjected to unidirectional rotatory habituation. Before and after the habituation a caloric test was carried out and the results of these tests were compared in order to establish whether the habituation had produced changes in the mode of reaction of the two labyrinths in the same way as had been shown earlier through monaural caloric habituation. This proved to be the case. In nine persons there was a directional preponderance to the right, whereas five showed generally diminished vestibular reactions. In one subject a spontaneous nystagmus to the right appeared. Ten persons showed a secondary nystagmus to the right after irrigations which produced nystagmus to the left. Nine cases presented, after the habituation, a characteristic dysrhythmia, mainly in connection with nystagmus to the right.

The two groups seem to be extreme cases with all gradations between them, depending partly on the mode of reaction of the subjects and partly on the strength of the stimulus used.

The results suggest that the reaction changes are not a consequence of a given method of stimulation but are a real expression of the way in which a habituation is developed within the vestibular organ.

The research of the last fifty years has shown that many of the so called reflexes may be profoundly and more or less permanently modified through repeated elicitation. Numerous investigations with both human subjects and animals have demonstrated that the vestibulo-ocular reflex, nystagmus, too, can be influenced in this way. The first researcher to elucidate this problem by experiment was Abels (1906), who was interested in the phenomenon of seasickness. He rotated pigeons in one direction several hundred times daily for several consecutive days and found that *in the rotating direction* the nystagmus progressively diminished, whereas when the pigeons were rotated in the opposite direction it remained largely unchanged. He considered that the change arose in certain parts of the central nervous system and that it might represent a positive and useful kind of adjustment to new and unusual circumstances.

Bárány (1907) found that professional dancers who usually rotated only in one direction had a nystagmus which in that direction was 10 sec shorter

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Department of Oto laryngology Karolinska Sjukhuset
Stockholm 60, Sweden

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Bárány (1907) found that professional dancers who usually rotated only in one direction had a nystagmus which in that direction was 10 sec shorter

than the normal 41 sec whereas after rotation in the opposite direction it was 10 sec longer He found no change in the duration of nystagmus if the dancers were accustomed to rotate in both directions Barany considered that in these cases only the sensation was reduced These results received support from later investigations made by Wintermute (1909)

Guttich (1914) performed similar experiments and demonstrated a marked decrease *in the duration of nystagmus*

Jones (1918) and Fisher & Babcock (1919) carried out repeated turning tests on human subjects according to the technique of Barany but were unable to show any reduction in the duration of nystagmus These experiments had been made in order to disprove the assertion of American psychologists that acrobats and equilibrists lose their nystagmus as a result of training This discussion aroused wide interest and stimulated a number of researchers to occupy themselves *with the problem Griffith (1920) investigated 17 persons* whom he caused to make five rotations in each direction daily a total of 15 such tests usually *being made On average he found a reduction of nystagmus* duration by 79 per cent The same reduction still remained when the subjects were examined after 1 8 weeks

Maxwell *et al* (1922) rotated rabbits daily during *22* days and obtained a marked reduction both in nystagmus duration and in the number of beats A caloric test after the habituation however gave entirely normal values

Dodge (1923) rotated himself 114 times daily for 6 days in an anticlockwise *direction He found* that towards the end of the experimental period nystagmus had practically disappeared and instead undulatory eye movements *had appeared After this habituation rotation in the opposite direction* showed that there was a 50 per cent transfer to the other direction

The same results were obtained by Holsopple (*1923*) with four persons who were repeatedly rotated in the same direction A clear response decline was demonstrated but no change occurred for rotation in the opposite direction

Mowrer (1932 1934) studied head nystagmus in pigeons after rotation in both directions and in only one direction In the former case the postrotatory nystagmus diminished in both directions When the pigeons were rotated in only one direction with an interval longer than the rotation time he obtained a greater reduction in postrotatory nystagmus for the direction in which the pigeons were *rotated than for the opposite direction If* on the other hand the rotation time was longer than the interval the result was the contrary Concerning the reasons *for the results Mowrer mentions the views of other* researchers but himself abstains from any explanation

Hood & Pfaltz (1954) *holding that earlier researchers in the field had* used in their rotation experiments stimuli which were too strong set out to study the problem with the use of a new *rotation method consisting of an* acceleration of 5°/sec² for 10 sec followed by constant velocity for 60 sec Finally the chair was decelerated at 5°/sec² *The experimental animals*—rabbits—underwent two such tests in each direction with 1 min interval

between each test The results showed a clear response decline Two weeks rest produced no recovery The experiments were therefore continued for an additional two weeks when the response declined still further to a final level of 85 per cent In another series of experiments it was shown that the frequency of application of the tests is of relatively little importance in determining the course of the response decline The authors considered *that the response decline* was due to a complex central process

McCabe (1960) investigated figure skaters before and after a training period and found that neither a rotation test nor a caloric test produced any nystagmus after the end of the training period

The present authors having studied vestibular habituation through caloric irrigation and obtained two different types of response, one with directional preponderance and one with reduced duration of nystagmus bilaterally, decided to investigate whether the same result could be obtained through another type of vestibular stimulation namely repeated rotation in one direction

MATERIAL AND METHODS

For the experiments there were used 14 members of staff without any vestibular disturbances Before habituation each subject underwent a *caloric* test *ad modum* Fitzgerald & Hallpike (1942) in order to establish whether he had normal vestibular reactions With a view to obviating a tendency to habituation resulting from the initial examination the sequence *of the tests* was such *that* each consecutive irrigation produced nystagmus in the direction opposite to that in the preceding test After the caloric test the subject was seated in a rotation chair (Stille-Werner) with his head *secured in a* holder and inclined forward 30°

The procedure of habituation was that the patient was rotated each time to the right with an acceleration *of 0 5°/sec² until the* chair had attained a velocity of 90°/sec This speed was kept constant for 3 min after which the chair was immediately stopped and the postrotatory nystagmus was recorded electronystagmographically When the reaction had ceased the subject rested for 5 min and the rotation was then repeated The same stimulation was applied to each subject 10-12 times

After this rotatory habituation to the right a final caloric test was carried out in order to obtain a comparison with the vestibular reaction before habituation

After each stimulation the nystagmus was recorded with an eight channel nystagmograph (Schwarzer) with two derived and rectified channels one for the slow phase and one for the rapid phase This provides good possibilities of observing the last nystagmus beat a very important matter in these experiments On another channel (time *constant 1* sec) with maximal amplification (50 microvolt = 1 cm) the nystagmus course was reproduced in the customary way without derivation However in certain subjects this high

amplification produced disturbances and an attempt was made to obviate this by recording on a further channel with somewhat lower amplification. The recording took place with closed lids.

RESULTS

During the progress of the habituation through repeated dextrorotatory stimulation the recording of postrotatory nystagmus showed that all the subjects gradually acquired a reduced nystagmus duration.

When, after the conclusion of the habituation, the caloric tests made before and after the experiment were compared, characteristic changes in the mode of reaction in the two labyrinths were found. One subject had acquired a spontaneous nystagmus to the right. Eight subjects had a directional preponderance to the right and they were therefore put together in one group (Group 1). With these subjects the posthabituation caloric test showed a longer nystagmus duration for 44° in the right ear and 30°C in the left ear,

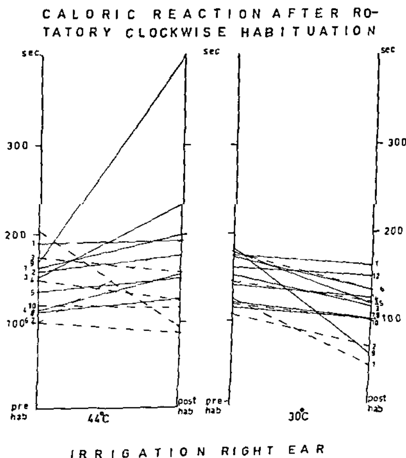


Fig. 1. Caloric reaction after rotatory clockwise habituation. Irrigation right ear. Group 1 (continuous line): Nystagmus duration increases to 44° but decreases to 30°. Group 2 (broken line): *Nystagmus duration decreases to 44° and 30°.*

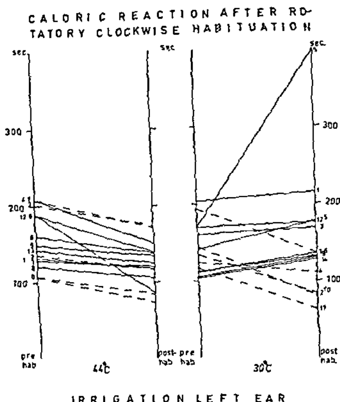


Fig. 2. Caloric reaction after rotatory clockwise habituation. Irrigation left ear. *Group 1 (continuous line)*. Nystagmus duration decreases to 44° but increases to 30°. *Group 2 (broken line)*. Nystagmus duration decreases to 44° and 30°.

whereas the duration was shorter for 44°C *in the left ear* and 30°C in the right *ear* (Figs. 1 and 2). The remaining five subjects showed a shorter nystagmus duration for both cold and hot water irrigation in both ears. These subjects were therefore put together in another group (Group 2).

Before habituation the subjects had not shown any signs of *dysrhythmia*, but after habituation nine of them developed a typical dysrhythmia after irrigation of the left ear at 30°C and of the *right ear at 44°C*. Two of these persons had a general dysrhythmia *after all irrigations*. A further two subjects had dysrhythmia *only for hot water* in the right ear or cold water in the left ear.

After habituation 10 subjects had a secondary *nystagmus to the right* after irrigation of the left ear at 44°C and of the *right ear at 30°C*, this could not be shown before the habituation.

Another interesting observation was *that* upon irrigation of the left ear at 30°C or of the *right ear at 44°C* three persons showed after habituation an absolute increase *of nystagmus frequency*, compared with the same

results before habituation. Two cases showed a reduction in frequency after irrigation of the left ear at 44°C.

Apart from the experiments already reported, some experiments were also conducted in which the initial stimulation was either lower or higher than that generally used, viz. 90°/sec. Four persons underwent the same experiments as the other subjects but the chair was stopped when a speed of 30°/sec. was reached. In none of these cases was it possible to show any signs of habituation after 10 clockwise rotation experiments. With another series consisting of three persons the chair was rotated up to a speed of 120°/sec. before being stopped. All these subjects showed results corresponding to Group 2, namely a general reduction of nystagmus duration for both cold and hot water.

DISCUSSION

The investigation has shown that after unidirectional rotatory habituation human subjects have characteristic changes in the reaction of the two labyrinths to a subsequent caloric test. As these changes entirely agree with those obtained after monaural caloric habituation (Fluur & Mendel 1962) this indicates that the reaction changes are not a consequence of a given method of stimulation but are a real expression of the way in which a habituation develops in the vestibular organ.

The variability in the changes in Groups 1 and 2 suggests that these two groups represent two extremes between which there are all gradations, as also appears from Figs. 1 and 2. One extreme is case No. 9, who after habituation had such a pronounced activity difference between the two labyrinths that a spontaneous nystagmus arose; the other extreme is shown by case No. 11, where the reactions of both vestibular organs diminished by about 50 per cent.

As after monaural caloric habituation there appeared in the present investigation both dysrhythmia and secondary nystagmus, both with a definite pattern of manifestation which seems to be easily capable of being covered by the explanation given in an earlier work (Fluur & Mendel 1962). The same is the case with the frequency increases observed after irrigations which produce nystagmus to the right.

The results obtained in Group 1 after habituation can be explained by the occurrence, under the influence of the efferents, of an increased hyperpolarization pressure in the left labyrinth and a raised depolarization pressure in the right labyrinth. It is then much easier for an ampullofugal endolymph flow in the left horizontal semicircular duct to increase an already existing hyperpolarization and therefore to give a longer duration on cold water irrigation. On the other hand it is more difficult for an ampullopetal flow in the same semicircular duct to reach the stimulation threshold, since it has first to overcome the increased potential difference before the depolarization and the action potentials can come into operation (in order to establish this

threshold measurements have been made and these will soon be published). In the right horizontal semicircular duct the situation is precisely the reverse. Owing to the increased depolarization pressure the stimulation threshold is reduced and depolarization comes more easily into operation upon an ampullopetal flow in connection with hot water irrigation. This is also the explanation of the fact that, upon hot water irrigation of the right ear, an *absolute frequency increase* of the nystagmus beat was obtained. The number of action potentials will naturally be considerably greater than was the case before the habituation.

For the same reason it is more difficult for an ampullofugal flow in the same semicircular duct to bring about a hyperpolarization and it therefore produces a shorter nystagmus duration after cold water irrigation.

Thus a habituation seems to develop along the following lines. If the established activity difference is sufficiently great, a spontaneous nystagmus arises, in this case to the right. If the difference does not reach this level, no spontaneous nystagmus arises and instead a secondary nystagmus to the right is produced after irrigations which primarily produce a nystagmus to the left. The difference in activity also exhibits itself occasionally in the form of an absolute increase of the nystagmus frequency if the nystagmus beats to the right. The investigations have also shown that dysrhythmia arises almost solely with nystagmus to the right. The interpretation of this phenomenon may be that the above mentioned frequency increase is so great that a block is periodically produced, giving the curve of this dysrhythmic appearance. If this block becomes manifest, a permanent inhibition will arise not only for nystagmus to the right but also for nystagmus to the left, as indeed has *been shown in Group 2. It is probable* that certain cases belonging to Group 1 would pass over to Group 2 if the stimulation in connection with the habituation had been more intensive or if the number of stimulations had been *greater. This* hypothesis is supported, among other things, by the fact that habituation experiments made with an initial stimulation of 30°/sec instead of the present 90°/sec did not produce any signs of habituation. In these cases the stimulation seems to have been too weak to produce any habituation after only 10 rotation experiments. *Habituation* experiments at 120°/sec on the other hand showed in all cases results belonging to Group 2, which may be interpreted as meaning that in these cases the stimulus was too strong to produce results according to Group 1.

ZUSAMMENFASSUNG

Vierzehn vestibular normale Personen wurden mit Rotation in einer Richtung angewöhnt. Vor und nach der Gewöhnung wurden kalorische Teste gemacht und die Resultate davon verglichen. Dadurch wollte man feststellen, ob die Gewöhnung irgendwelche Veränderungen *in der Reaktionsart* der beiden Labyrinthe mitgebracht hatte, ähnlich wie schon bei der monauralen kalorischen Gewöhnung gezeigt worden *ist. Es stellte sich heraus*, dass dies der Fall war.

In neun Fallen erhielt man eine Nystagmusbereitschaft nach rechts, während fünf Personen allgemein reduzierte vestibuläre Reaktionen zeigten In einem Fall trat ein Spontannystagmus nach rechts auf Zehn Personen zeigten nach Spülungen, die einen Nystagmus nach links gaben, einen Sekundärnystagmus nach rechts In neun Fällen sah man nach der Gewöhnung eine charakteristische Dysrythmie, hauptsächlich in Verbindung mit dem Nystagmus nach rechts

Es scheint, als seien die beiden Gruppen die äussersten Gegensätze, zwischen denen man alle Übergänge finden kann Teils hängt es von der Reaktionsart der Versuchsperson, teils von der Stärke des verwendeten Reizes ab

Die Resultate deuten darauf hin, dass die Veränderungen der Reaktion nicht die Folge einer bestimmten Stimulationsmethode, sondern ein wahrer Ausdruck für die Entwicklung einer Gewöhnung im Vestibularorgan sind

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Department of Otolaryngology Karolinska Sjukhuset Stockholm 60 Sweden

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HABITUATION (ADAPTATION) IN THE MIDDLE EAR MUSCLE REFLEXES OF THE CAT

F. BLAIR SIMMONS and DANA L. BEATTY[1]
Stanford, Calif., U.S.A.

From the Division of Otolaryngology, Stanford University School of Medicine, Stanford

Habituation (adaptation) in the middle ear muscle acoustic reflex response of the cat is described which has been observed as altering reflex threshold sensitivity by as much as 50 db and as affecting continuous contractions to an equally impressive degree. These observations (and their ramifications) are offered as one explanation for so called "species differences" in reflex sensitivity and as a basis for suggesting that similar effects probably also occur in man.

INTRODUCTION

Middle ear muscle reflex sensitivity differences have often been reported between man and some common laboratory animals. For instance, de Nó & Harris (1933), Eliasson & Gisselsson (1955) and Simmons (1959) have reported thresholds of 30–40 db SPL in the cat or rabbit while the usual sensitivity measurements for man seem to be between 75 and 95 db SPL (Lindsay *et al.* 1936, Jepsen 1951, Møller 1961). Such differences ought to be explicable without the need for assuming an unlikely fundamental difference in the compositions of the lower level auditory systems of the various species measured. Indeed, the rather surprising range of reflex sensitivities reported not only by different experimenters but often by the same experimenter within a single experimental population serve to heighten the suspicion that some unrecognized variable in all species is at work.[2]

Effects on reflex activity due to one possible variable, habituation (adaptation), are to be reported here for the cat. In this species (*Felis domesticus*) the opportunity for observing habituation is especially good. In the cat's natural environment, the sounds common to an audiometric laboratory

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(pure tones and random noise) are unknown. To this (in the case of the awake animal) add the initial exposure to the laboratory environment itself, and the test situation is as initially conducive to minimal habituation as could be desired. Habituation will occur, however, if the same cat is continually re-exposed to the same set of circumstances over a long enough period of time. Furthermore the same "degree" of habituation will require longer or shorter periods of time for different animals.

METHODS

In our laboratory we have recently had what might be considered an ideal set of circumstances for observations of *habituation phenomena*: two environments of unequal familiarity, both employing the same auditory stimuli, pure tones. In one environment complete habituation or adaptation may be presumed to have occurred during an almost daily exposure for up to six months. During this time the animals were trained to make threshold discriminations in a shuttle box, and once these were learned, to maintain them. In the second environment, habituation was usually deliberately avoided by *keeping awake animal* test sessions short, infrequent, and followed immediately by administration of a general anesthetic (Nembutal). This second environment was used *primarily* for measuring cochlear electrophysiological responses to tones of the same frequencies used in the first environment. (The basic protocol of the over-all experiment has been published elsewhere (Simmons & Beatty, 1962*a*).)

In addition to the main purpose of the study, middle ear muscle reflex measurements were also obtained from awake animals, restrained and unrestrained, and in both environments, through electrodes permanently im*planted on the round window or in the middle ear muscles*, or both. Reflex activity was determined either directly by electromyography or indirectly by measuring the attenuation of the cochlear microphonic (CM) produced by muscle contractions (Simmons, 1959), or by both methods. In most instances the reflex responses were measured to a standardized series of test tones of graded intensity—low to high—and at several different frequencies, always in the same order.

RESULTS

Reflex responses measured within the threshold discrimination test environment provided the initial impetus for examining closely the effects of habituation. In three animals little or no reflex activity was observed at stimulus intensities 80–90 db SPL and at least 75 db above each animal's auditory *threshold*. (These three cats had all sustained varying degrees of threshold elevation due to sound trauma which occurred a month or more before the reflex measurements. According to published reports, however,

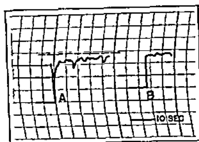


FIG 1 Middle ear muscle reflex attenuation of cochlear microphonic in different test environments *A*—electrophysiological *B*—behavioral The sound stimuli were continuous 1 kc tones of approximately equal intensity (95 db SPL) The amplitude of the CM response to the same tone with the reflex deactivated by a general anesthetic is the dashed line drawn above the *A* measurements (A similar anesthetized measurement was also obtained in the behavioral environment but could not be as exactly placed because standing waves in the open field behavioral test environment introduced a probable error of measurement ±3 db) Each horizontal line in the chart paper equals 7 5 db of CM amplitude

these losses should not have affected reflex activity (Metz, 1952)) While this lack of reflex response might not have been surprising in itself, it was impressive to find, in each instance, that the very same intensities and frequencies presented in the other environment (electrophysiological) evoked large degrees of middle ear muscle response!

Fig 1 shows one such set of comparative measurements These were obtained from the same animal on the same day *B* shows CM amplitude response to a 90 db SPL tone in the behavioral test environment *A* shows the same measurement in the electrophysiological environment

At first such marked differences in reflex responses to approximately equal test tones caused a critical reappraisal of the electrophysiological methods employed—in search primarily of possible artifacts such as effects of the cat s pinna on the sound field generated by the insert receiver None was found (Simmons 1962*b*) Failure to find artifacts, plus the later support of concomitant EMG measurements, led to the conclusion habituation

The reflex response measurements in the threshold test environment were however, one time for each animal For technical reasons, all were obtained from well-trained animals which did not exhibit excessive spurious movement or false responses Consequently, the gradual development of habituation was only observed in the more convenient electrophysiological test environment

A gradual development of reflex habituation is shown in Fig 2 In this figure the reflex response to a 1 kc tone at about 75 db SPL is shown for one animal as measured at intervals over a two month period Early, reflex responses were marked Then as the number of tests increased, reflex activity diminished until the 27th day After this test no further testing was done until the 60th day, when some evidence of return of reflex activity (dishabituation) can be seen

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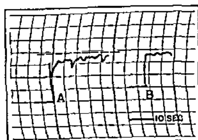


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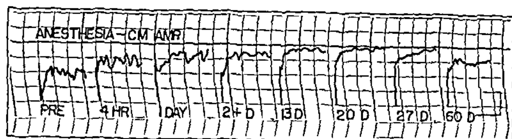


Fig 2 Habituation of the middle ear muscle reflex Reflex attenuation of the CM amplitude for a 75 db 1 kc tone—as compared to muscle deactivated (anesthetized) amplitudes (dashed line)—is shown for a series of tests over a two month period The time labelling refers to days after a traumatic sound exposure (see text) The inkwriter tracings were redrawn from original data adjusted for equal amplitude of anesthetized CM CM amplitude equals 7.5 db/horizontal chart line

Aside from the general nature of the diminished reflex activity it may also be important to note that even though the initial reflex attenuation of the CM was still more marked than the sustained attenuation the relaxation was also more rapid If reflex activity had been judged at only one point in time for instance 2–3 sec after onset of the tone on the 20th day little or no activity would have been observed Yet the same reflex attenuation during the same stimulus interval three weeks earlier or 40 days later was considerably stronger

To obtain these measurements the rigidity of the previously mentioned protocol was relaxed the duration of test sessions increased and awake measurements were not always followed immediately by a general anesthetic The measurements from this particular animal represent the most marked degree of habituation noted However this animal was also the most extensively tested and the alterations are sufficiently profound to support the probability of a correct evaluation of the results typified in Fig 1

The time reference of Fig 2 relates to a traumatic sound exposure from which the cat incurred a permanent 25 db loss at 1 kc Though the loss was initially greater than this (75 db immediately post exposure) recovery was maximal after the second post exposure day Thus it cannot be presumed to account for subsequent loss in reflex activity which if anything might have been expected to be greatest at the 3 hr post exposure measurement

Habituation effects are however not necessarily limited to a gradual diminution of reflex responses over days or months Further observations on the extent of habituation possible during a single test session were obtained from other animals who were not part of the original experimental population Some of these cats were presented with an almost continuous tone for periods of up to 2 hr Others received regularly or irregularly repeated short (1–5 sec) bursts of the same tone Using these stimuli it was possible to alter reflex thresholds by as much as 30 db (from 55 db to 85 db SPL) at 1 kc At no time were stimulus intensities great enough to produce end organ fatigue or other phenomena a[illegible]

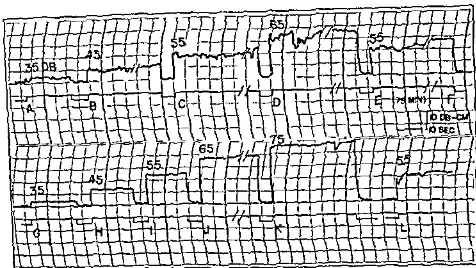


FIG 3 Habituation in middle ear muscle reflex activity occurring during one prolonged test session which included continuous stimulation for 75 min with a 55 db SPL 1 kc tone Tracings shown are inkwriter recordings of CM amplitude generated by the 1 kc stimulus at the intensities specified To conserve space segments of continuous recordings have been deleted as indicated by —/ — Each horizontal division in the chart paper equals 7 5 db of CM amplitude

shift Indeed one requirement for obtaining maximal habituation is avoidance of more intense sounds (with brief durations) Their introduction can temporarily increase reflex sensitivity (Simmons 1960)

Changes in reflex activity illustrating such habituation effects are shown in Fig 3 The measurements shown are again inkwriter recordings of the amplitude of the CM response to a 1 kc tone They were obtained from an experimentally naive cat using the following protocol A tone was initially introduced at 35 db SPL (*A*) and remained on for about 20 sec After a 7 sec silent period the tone was re presented at 45 db (*B*) for 50 sec followed by a tone at 55 db (*C*) for 3 min and finally by one at 65 db (*D*) for 70 sec Then the 55 db tone was re introduced and left on continuously for about 75 min (*E* to *F*) Twenty five sec after discontinuing the 55 db tone the initial 35 db tone was re introduced (*G*) followed by tones at the other intensities (*H* *I* *J*) and by an additional more intense test tone at 75 db (*K*)

The degree of habituation allowed by the long presentation of the 55 db tone is evident in the almost square contour of the CM response to the second set of test stimuli Before the 75 min tone reflex activity can easily be detected even at 35 db where CM amplitude was attenuated for a brief interval (about 2 sec) immediately after introduction of the stimulus Afterwards it is difficult to detect any initial reflex response until the stimulus intensity is somewhere between 65 and 75 db and even this is remarkably little

That such reflex changes represent habituation rather than some other phenomenon such as fatigue is relatively easy to demonstrate Reflex altera

tions like those in Fig. 3 can be dishabituated by changing the test environment or by presenting novel reflex stimuli. (The final tracing (I) in Fig. 3 is an example. Again, a 55 db tone was introduced, but after the animal had been briefly exposed to several tones with frequencies other than 1 kc. Return of this previously habituated reflex response can be seen.) Also, habituation to long presentations of continuous tone can be at least partially prevented by intermittently interposing additional constantly changing sounds either in the same or in the opposite ear.

Furthermore, it is unlikely that any end organ or muscle fatigue would result at the stimulus intensities used. Reflex responses to non-auditory stimuli (such as a puff of air) can be elicited during depression of auditory reflex responses. And, as judged by electrophysiological indices, fatigue within the cochlea does not appear to manifest itself in alterations of reflex response until stimulus intensities exceed 95 db. The effects of very long stimulation of this sort with more intense tones have not been studied in detail. Fatigue effects which have been examined, however, show both an initial depression and a recovery pattern with time that are quite different from habituation. As a partial example, and without going into detail, to obtain the effects shown in Fig. 3 by fatigue (or damage to the cochlea) the animal's auditory threshold acuity would have had to be depressed at least 70 db at 1 kc.

DISCUSSION

That the middle ear muscle acoustic reflex is capable of habituation is not surprising, nor is the observation of such habituation new. Kobrak, Lindsay & Perlman (1941), for instance, correctly attributed to habituation the gradual relaxation of reflex response to continuing stimuli when they observed that a re-intensified contraction could be produced either by superimposition of a second stimulus, or by momentary interruption of the original stimulus. Since then, this has been confirmed many times in man and in experimental animals.

The observations of habituation reported here, while perhaps resting on the same principles, are different in magnitude and duration than those of earlier studies. They show not only that habituation occurs for short duration stimuli (Fig. 1 A) but also that it may accrue in a number of other circumstances—in multiple test sessions (Fig. 2), during one prolonged session (Fig. 3), or in different degrees in the same subject, depending upon environment as well as past experience (Fig. 1).

The impressive changes in reflex sensitivity (40–50 db) and (in diminished degrees) in sustained contraction seen under such circumstances are often of the same order of magnitude as species differences. For example, the same animal may have a reflex threshold at 40 db SL (1 kc) in the absence of habituation, and a threshold at 80–90 db SL when habituated.

To this author, the presence or absence of habituation offers reasonable

grounds for a rational explanation of at least part of the variable nature of the reflex threshold, not only when comparing measurements from experimental animals with those from man but also when individual variability (in any one set of measurements) in either population is examined In man Møller indirectly acknowledges the presence of some such factor in relating reflex threshold to auditory threshold He completely avoids measuring both reflex threshold and short latency reflex responses—the two indices which should be most susceptible to the influence of habituation—to attain test retest reproducibility and better correlation

The proposed role of habituation does not completely clear the picture of differences in middle ear muscle sensitivity among species or between individuals even though it may make possible a more rational approach to such differences The question of the contribution of differences in auditory threshold between species remains The cat for instance has more sensitive hearing than man by about 10 db at 1 kc and even better sensitivity at higher frequencies (Elliott 1960)

However in spite of the possible effects of differences in auditory sensitivity the question of habituation remains Its presence demands a reconsideration (in any reflex determination) of the broader question What aspects of the auditory system are being measured by the commonly employed measurement techniques? To answer this at the level of the cochlea Perlman poses a direct relation with stimulation of the inner hair cells rather than the excitation of the more sensitive outer hair cells This is worthwhile considering and may account for some of the findings of Metz on reflex measurements of damaged ears The cochlear considerations important as they may be do not allow escape from additional emphasis on potential major contributions from within the central nervous system portion of the reflex arc, and the factors (such as habituation) which govern its physiological continuity The best example of this additional influence comes from the apparently extensive work of Wersäll (1958) on rabbits His techniques most closely paralleled those of deNo but he reported a reflex sensitivity which was about 50 db poorer than this earlier study (40 *vs* 90 db) He also reported, among other things that there was no fundamental difference due to type of anesthesia , and that the observations made were only moderately influenced by artifacts due to the anesthetic agent. (The principal anesthetic used was a barbiturate whose major effect is suppression of the reticular formation and which has no gross electrophysiologically discernible effect on the intact cochlea (Simmons unpublished observation)) In addition to the sensitivity disagreement with deNo Wersäll s findings are totally contrary to those *in our laboratory*—whose major experimental tool is the normal awake cat Reflex activity in these animals is regularly attained at 40 db SPL agreeing with deNo *And* our most convenient method for eliminating reflex activity is by administering a barbiturate anesthetic While the dose used is admittedly larger than Wersäll s we have also administered graded intravenous doses of *Pentothal* (a thiobarbiturate) while

tions like those in Fig. 3 can be dishabituated by changing the test environment or by presenting novel reflex stimuli. (The final tracing (*I*) in Fig. 3 is an example. Again a 55 db tone was introduced, but after the animal had been briefly exposed to several tones with frequencies other than 1 kc. Return of this previously habituated reflex response can be seen.) Also habituation to long presentations of continuous tone can be at least partially prevented by intermittently interposing additional constantly changing sounds, either in the same or in the opposite ear.

Furthermore, it is unlikely that any end organ or muscle fatigue would result at the stimulus intensities used. Reflex responses to non-auditory stimuli (such as a puff of air) can be elicited during depression of auditory reflex responses. And, as judged by electrophysiological indices, fatigue within the cochlea does not appear to manifest itself in alterations of reflex response until stimulus intensities exceed 95 db. The effects of very long stimulation of this sort with more intense tones have not been studied in detail. Fatigue effects which have been examined, however, show both an initial depression and a recovery pattern with time that are quite different from habituation. As a partial example, and without going into detail, to obtain the effects shown in Fig. 3 by fatigue (or damage to the cochlea) the animal's auditory threshold acuity would have had to be depressed at least 70 db at 1 kc.

DISCUSSION

That the middle ear muscle acoustic reflex is capable of habituation is not surprising, nor is the observation of such habituation new. Kobrak, Lindsay & Perlman (1941), for instance, correctly attributed to habituation the gradual relaxation of reflex response to continuing stimuli when they observed that a re-intensified contraction could be produced either by superimposition of a second stimulus, or by momentary interruption of the original stimulus. Since then this has been confirmed many times in man and in experimental animals.

The observations of habituation reported here, while perhaps resting on the same principles, are different in magnitude and duration than those of earlier studies. They show not only that habituation occurs for short duration stimuli (Fig. 1.1), but also that it may accrue in a number of other circumstances—in multiple test sessions (Fig. 2), during one prolonged session (Fig. 3), or in different degrees in the same subject depending upon environment as well as past experience (Fig. 1).

The impressive changes in reflex sensitivity (40–50 db) and (in diminished degrees) in sustained contraction seen under such circumstances are often of the same order of magnitude as species differences. For example, the same animal may have a reflex threshold at 40 db SL (1 kc) in the absence of habituation, and a threshold at 80–90 db SL when habituated.

To this author the presence or absence of habituation offers reasonable

STAPEDECTOMY

Observations on 100 cases using an adipose tissue graft and steel pin prosthesis

B H Colman
Coventry England

Consultant E N T Surgeon Coventry Group of Hospitals

Experiences and conclusions drawn from a series of 100 consecutive stapedectomy operations utilizing an adipose tissue graft and steel pin prosthesis are described Eighty eight operations resulted in hearing within 10 db of the patient s pre operative bone conduction threshold Three patients had worse hearing after operation The period of observation was between one and three years Post operative difficulties and complications were minimal The method of reconstruction was found suitable throughout the wide variety of situations met in the series and reasons are submitted for having developed a personal preference for this technique Results of stapedectomy are nevertheless probably independent of the exact method of reconstruction favoured by individual surgeons

The concept of mobilizing or removing the stapes in order to improve the transmission of sound to the oval window is by no means new, only the limitation of such procedures to the treatment of otosclerosis and incorporation of them with various methods of ossicular reconstruction represent recent refinements

Stapes fixation as a cause of deafness was first reported by Valsalva (1735) who found in the dead body of a deaf man that the reason for his deafness lay in the fact that the membrane around the base of the stapes had hardened on to the bony substance to form one continuous bone with the base of the stapes and the edge of the oval window and so made it impossible to move up and down any more

Interest was rekindled by Toynbee (1841), who finally collected 189 such cases but the earliest surgical attempts to relieve deafness due to ossicular fixation were probably those of Kessel (1876 1877) Blake (1892) appears to have taken a more critical and logical approach than his contemporaries he expressed the view that many of their operations which had been directed mainly at the drum malleus and incus were unscientific and violent and suggested that any improvement was due to accidental mobilization of the stapes the ossicle primarily at fault in cases of non suppurative conductive deafness He felt that complete removal of the stapes was superior to mobilization but admitted frequent difficulty from crural fracture

However two factors undoubtedly had a dampening effect on the enthusiasm

observing reflex activity. In such circumstances, the decreased reflex response (threshold and suprathreshold) is marked, approximating Wersall's "normal reflex sensitivity".

The objective of the foregoing comparisons is not to point out an error due to artifact, but rather to demonstrate lucidly that strong attention must be given to central nervous system influences, which by classical definitions are considered only indirectly related to brainstem auditory systems

A final glance at Fig 3 prompts one additional question with particular reference to current methods of impedance or impedance change measurements of reflex activity in man: Does the presence of the carrier tone contribute to auditory adaptation?

RÉSUMÉ

L'état habitué (l'adaptation) pour la réflexe réponse acoustique des muscles de l'oreille moyenne est décrit Cet état a été observé à changer la sensitivité initiale du réflexe (threshold) autant que 50 db, et à affecter également les contractions continuelles Ces observations (et leurs ramifications) sont offertes comme une explication des « différences entre les espèces », si dites, par rapport à l'acuité auditive — et comme une base pour suggérer l'événement des effets semblables dans l'homme

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Division of Otolaryngology, Stanford University School of Medicine, Stanford.

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of an adipose tissue graft and steel pin prosthesis a procedure which has been employed less frequently by European surgeons than the Shea operation in those patients in whom the stapes suprastructure has to be replaced by a foreign material to restore the continuity of the sound conducting mechanism The series deals with one hundred consecutive operations involving a total of 90 patients The patients were seen in the outpatient clinic by one of several clinicians diagnosed as suffering from otosclerosis and considered to be capable of improvement by surgery The cases were unselected and included patients with extremely poor bone conduction as well as patients with near normal Eighteen patients had previously had mobilization operations The technique closely followed that developed by Schuknecht (1960)

Experimental Basis

The experimental work on animals has been fully described elsewhere Studies on the tolerance of stainless steel and on tantalum wire reported by Schuknecht and Oleksiuk (1960) indicate that such wire is completely inert in the middle ear and becomes enclosed in a mucosal sheath In the six years that have elapsed since he first implanted stainless steel wire in the human ear Schuknecht (1963) has not observed intolerance

Adipose tissue was selected after an experiment by Colman (1960) in which various types of tissue were implanted across the oval window *after* total stapedectomy in cats Adipose tissue consistently gave the best type of membrane it persisted virtually unchanged except for the acquisition of an envelope of collagen tissue upon which endothelium and mucosa were superimposed The collagen was fully mature and the fat cells appeared normal in respect of fat content and vascular supply (Figs 1 and 2)

The response of the internal ear to stapedectomy and the placement of a graft across the oval window has also been examined by Colman (1962*a*) Again the evidence suggests that adipose tissue is amongst the most satisfactory tissues available the neuro epithelial contents of the cochlea and vestibular labyrinth being normal in each animal with this type of graft

Notes on Technique

Local anaesthesia has always proved satisfactory even in patients who initially were apprehensive Certain otologists have expressed a preference however for general anaesthesia and this method is currently on trial

The lobe of the ear provides good adipose tissue a piece of which is trimmed to the approximate size of the oval window *i e* 2 × 3 ——

... and a small amount of perilymph is aspirated Subsequent footplate work is done in air not in perilymph and the risk of stimulation injury to the cochlea thereby minimized The type of

of otologists of this time. Firstly, Politzer (1894) in describing the pathology and histology of stapes fixation emphasized the impossibility of achieving footplate removal if the disease was advanced, since crural fracture would occur first. Mobilization he regarded as futile because of the inevitable bony reunion. He felt that "in spite of the great advance in otology in recent years the disease will not be controlled till the causative bone disease can be controlled". In this respect the answer to otosclerosis is little nearer even today in spite of ingenious methods of surgical relief of the main symptom.

Secondly, in spite of many encouraging results a number of otologists had experienced disaster, and reports from the International Congress of 1894 in Rome quoted by Politzer and by Leland (1895) indicate that total loss of hearing was becoming recognized as a significant hazard. Siebenmann (1900) at the next congress finally brought this era to an end by his condemnation of stapes surgery, the effects of which were felt for the next half century and which were reiterated by Sourdille as late as 1937.

In spite of the outstanding achievements of Sourdille, Holmgren and Lempert in establishing lateral canal fenestration as a safe and certain procedure, oval window surgery has once again become the focus of intense interest. It is now generally accepted that the acoustic advantages of utilizing the transformer mechanism of the middle ear are so great that operations designed to re-establish sound conduction to the oval window are the treatment of choice. Shambaugh (1952) in his series of fenestration operations found the residual middle ear hearing loss averaged 25 db for the speech frequencies, and recent work by Lawrence (1960) confirms the 25 db advantage provided by the intact middle ear mechanism.

Furthermore, a fenestration cavity undoubtedly imposes a permanent disability on the patient. It calls for regular attention indefinitely and in a certain proportion, maybe as high as 13 per cent according to Hall (1958), infection and persistent otorrhoea occur. Even a well-healed cavity imposes certain limitations on the patient, especially in sport and recreation.

Stapes mobilization proved attractive in avoiding certain of these disadvantages and occasionally gave excellent long-term improvement in hearing with complete eradication of the conductive deafness. Subsequent developments have been designed to secure this type of result more often. As in the last century, mobilization has led to partial and then total stapedectomy, combined with a variety of reconstructive techniques. The footplate can be replaced by vein (Shea, 1956), connective tissue or adipose tissue (Schuknecht, McGee and Colman, 1960) or by a film of gel-foam (House, 1960). Portmann (1958) prefers to retain the stapes head, neck and crura whenever possible, whereas Zollner (1960) prefers to utilize a bone strut cut from the mastoid. Alternatively a foreign material can be used, such as a plastic columella (Shea, 1958) of Polythene, Portex or Teflon, or a pin of tantalum or stainless steel wire (Schuknecht, 1960). Each of these methods, combinations and modifications has its adherents and its critics.

In this series of total stapedectomy operations reconstruction was by means

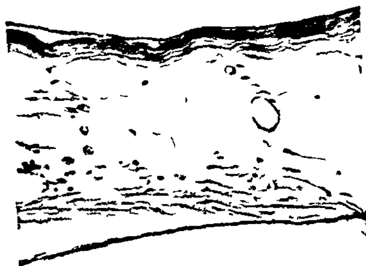


Fig. 2 High power view of graft The surfaces of the graft have a collagen envelope upon which internal ear endosteum (above) and middle-ear mucosa (below) are superimposed

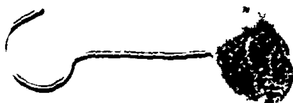


Fig. 3 The fat graft and steel pin prosthesis The overall length is approximately 4 5 mm

adipose tissue graft in a reopened ear has confirmed the attractive appearance found in the experimental animal (4) Technically it has been found easier to utilize a steel pin in those patients with a deep narrow oval window recess or a low and dehiscent facial nerve The pin can easily be modified for patients in whom previous surgery has produced a necrosis of the incus (5) The semi fluid adipose tissue immediately moulds itself accurately to the shape



Fig 1 Transverse section of oval window area of cat after stapedectomy and insertion of an adipose tissue graft The middle ear space is below, the vestibule of the labyrinth above The basal turn of the cochlea is just included at top left

footplate hooks used is largely a matter of personal preference, they must be inserted and manipulated with gentle but deliberate movements and with the thought constantly in mind that the cochlear duct is only 0 3 mm from the anterior edge of the window as Anson & Bast (1958) have demonstrated in their important anatomical studies The aim, nevertheless, should be 100 per cent removal of the footplate The prosthesis is inserted immediately and pressed into position until the wire loop can be closed over the long process of the incus The details of the operation as carried out in these patients have been described in an earlier paper (Colman, 1962*b*)

The patient is usually kept in bed for three days, in hospital for seven days and advised to be fairly inactive for another week

A preference for the steel pin and fat graft operation has developed for the following reasons (1) The pin is securely fixed at both ends and cannot easily lose contact with incus or graft (2) The attachment of the pin to the incus relieves any tension on the graft the graft simply being suspended in the window Both Shambaugh (1960) and Zollner (1960) have stressed the possibility of pressure necrosis with polythene tubing on vein and have attributed certain cases of late labyrinthitis to it (3) The appearance of the

consists of cases with an initial bone conduction level of 0–15 db group B 16–25 db group C 26–35 db and group D more than 35 db above the normal threshold

These groups correspond fairly closely to those described by Shambaugh & Carhart (1951) in the selection of cases for classical fenestration and represent respectively cases which are ideally suitable, not ideal but still well suited, of doubtful or borderline suitability and totally unsuitable The thick vertical line in each case represents the rise in hearing the short horizontal bar represents the initial bone conduction level The greatest gain was 63 db in a patient with a middle ear deafness of 65 db before operation The average gain in those patients improved by operation was 35 7 db excluding those 14 patients in the most unsuitable group (bone conduction worse than 35 db) 68 out of 86 operations (79 per cent) resulted in hearing at 30 db or better (British Standard)

Patients worsened by Operation

Three patients sustained deterioration of hearing from operation all due to sensori neural degeneration They are indicated in the chart by the arrowed dotted lines and are lettered as follows

A A patient not personally examined before operation who had an initial air conduction threshold of 73 db of which probably only 13 db represented a middle ear deafness certain discrepancies were present in the audiometric tests He had an oval window obliterated by dense thick bone needing much work with the trephine till entrance was made His already extremely poor hearing in the ear became worse and the ear remains functionally useless

B This patient heard well till an attack of influenza six months after operation He then sustained a moderate hearing loss for the uppermost frequencies but speech reception and discrimination were still good At 11 months after operation sudden and severe loss of hearing in the ear occurred It may be significant that his graft was rather small and was supplemented by gel foam It is now known that this material sometimes produces a membrane which can be dangerously thin

C A patient with very good bone conduction who sustained the operative complication of floating footplate This complication has been found more likely to occur after a previous temporarily successful mobilization the entire footplate usually of the thick biscuit type, becomes free and floats on the perilymph It is extremely difficult to insert a hook deep to it without risk of severe cochlear damage and the intact footplate is too large to be extracted between the lips of the oval window This complication is probably the most difficult with which the surgeon can be faced In retrospect it would perhaps have been wiser to have abandoned the operation and later carried out a classical fenestration The patient's initial average loss of 45 db

of the window and adheres. This moulding property at the time of implantation is a particular asset; whether the graft eventually becomes simple connective tissue in certain cases is not of significance.

RESULTS

In this series of operations the minimum follow up has been one year and the maximum three years. Two patients have died (coronary thrombosis and bronchopneumonia at 12 and 20 months respectively after operation) but otherwise no patients have been untraced.

As in most methods of stapedectomy hearing improvement is rapid in the first three weeks but often continues for as long as three months. Shea (1961) has stated that bony reclosure of the oval window which occurs in about 3 per cent of cases is usually early and *occurs most often in those patients with* total obliteration of the oval window. It has not occurred in this series though is to be expected perhaps in young patients with extensive and active disease. Portmann (1961) has also expressed the view that any recurrence of middle ear deafness is nearly always in the first four months and that the hearing gain at four months can probably be regarded as permanent. Continued observation of a series previously reported (Colman 1962*b*) the results of which are incorporated in the present paper, supports this view. *The only late failure* was due to sensori neural degeneration and will be described later (Case B).

Analysis of the results was made in the customary way by *comparing the* final air conduction threshold with the initial bone conduction threshold *taking the average for the three speech frequencies i.e. 500, 1000 and 2000* cycles per second. For practical purposes the initial bone conduction threshold can be *regarded* as representing the highest level of hearing that can be hoped for though sometimes the result is even better because of an apparent improvement in sensori neural function resulting from operation.

Three patients were made worse by operation and will be described later. Of the operations resulting in improved hearing only nine patients had a residual air bone gap greater than 10 db and these include a patient in both of whose ears otosclerosis was complicated by fairly dense adhesions and a necrosis of the incus from healed suppuration.

The overall results for the improved patients are as follows:

Residual air bone gap	No. of patients
greater than 15 db	5
between 15 and 11 db	4
between 10 and 6 db	19
between 5 db or less	34
Air conduction better than bone conduction	35

The individual results are summarized in the adjoining tables (Figs 4–7) and grouped according to the method of Ewert & Shea (1960). Group A

consists of cases with an initial bone conduction level of 0–15 db, group B 16–25 db, group C 26–35 db and group D more than 35 db above the normal threshold.

These groups correspond fairly closely to those described by Shambaugh & Carhart (1951) in the selection of cases for classical fenestration and represent respectively cases which are "ideally suitable", "not ideal but still well suited", "of doubtful or borderline suitability" and "totally unsuitable". The thick vertical line in each case represents the rise in hearing, the short horizontal bar represents the initial bone conduction level. The greatest gain was 63 db in a patient with a middle ear deafness of 65 db before operation. The average gain in those patients improved by operation was 35.7 db. Excluding those 14 patients in the most unsuitable group (bone conduction worse than 35 db), 68 out of 86 operations (79 per cent) resulted in hearing at 30 db or better (British Standard).

Patients worsened by Operation

Three patients sustained deterioration of hearing from operation, all due to sensori-neural degeneration. They are indicated in the chart by the arrowed dotted lines and are lettered as follows:

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B. This patient heard well till an attack of influenza six months after operation. He then sustained a moderate hearing loss for the uppermost frequencies but speech reception and discrimination were still good. At 11 months after operation sudden and severe loss of hearing in the ear occurred. It may be significant that his graft was rather small and was supplemented by gel foam. It is now known that this material sometimes produces a membrane which can be dangerously thin.

C. A patient with very good bone conduction who sustained the operative complication of "floating footplate". This complication has been found more likely to occur after a previous temporarily successful mobilization: the entire footplate, usually of the thick "biscuit" type, becomes free and floats on the perilymph. It is extremely difficult to insert a hook deep to it without risk of severe cochlear damage and the intact footplate is too large to be extracted between the lips of the oval window. This complication is probably the most difficult with which the surgeon can be faced. In retrospect it would perhaps have been wiser to have abandoned the operation and later carried out a classical fenestration. The patient's initial average loss of 45 db

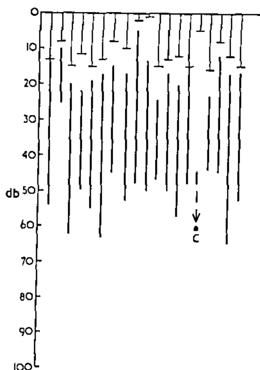


Fig 4 Group A patients

As described in the text, the patients are grouped according to their initial bone conduction level (short horizontal bars) The thick vertical lines indicate the improvement obtained and a dotted arrowed line indicates worsened hearing The scale is in decibels

Patients found to have complicating middle-ear scarring or necrosis are denoted by an asterisk Those patients lettered or numbered are discussed individually in the text

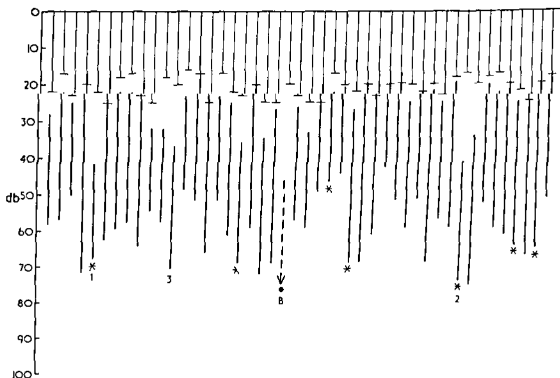


Fig 5 Group B patients

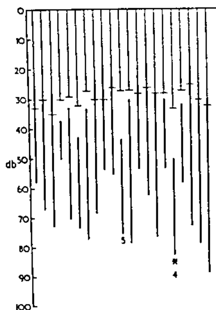


Fig 6 Group C patients

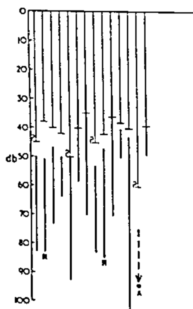


Fig 7 Group D patients

for air conduction is now 57 db most of the extra loss being at 2000 cps and with corresponding impairment of speech discrimination

Patients with a Residual Middle ear Deafness greater than 15 db

Although the majority of patients obtain hearing within 10 db of their initial bone conduction level and can be considered to have obtained a good hearing result a small number do not even come within 15 db In stapedectomy these cannot be considered perfectly satisfactory The following patients have to be included in this group in certain of them the reason is clear or was even anticipated before operation The numbers correspond to those on the charts

(1) A patient whose records of a previous mobilization operation described necrosis of the incus and extensive fibrosis in addition to an otosclerotic footplate He was offered further surgery in spite of this initial hearing level 68 db final level 42 db residual gap 20 db

(2) The same patient opposite ear Dense adhesions covered the incus stapes and pyramid The incus was intact Initial hearing level 75 db final level 41 db residual gap 24 db

A number of other patients with adhesions or necrosis of the incus are included in this series and are indicated on the charts by an asterisk It was generally known before operation that adhesions or necrosis or both were present and though a perfect result is not to be expected in such patients much can be gained from operation Necrosis can be overcome by inserting a suitable modified prosthesis but the denser any adhesions the greater is any residual conductive deafness

(3) An elderly patient with fairly good bone conduction who was found to have the oval window completely obliterated by very dense bone In the absence of a micro drill the trephine was used to make an entrance but after breaking a footplate hook in attempts to enlarge the opening it was decided to discontinue the operation rather than persist and thereby almost certainly produce cochlear damage A very small graft on a steel pin was inserted simply to restore the *status quo* rather than in the hope of obtaining improvement such was the apparent tightness of the prosthesis in the small opening obtained

Initial hearing level 71 db final level 37 db The residual gap of 17 is far better than was hoped for In spite of the small size of the window there is no evidence of recurrent deafness in the year since operation the bone is evidently in the completely healed stage

(4) The only patient in the series in whom re exploration was carried out Six weeks after the initial operation her severe middle ear deafness suddenly recurred The steel pin had slipped off the incus and was repositioned without difficulty For months afterwards hearing was maintained at about 10 db below the *bone conduction* level but recently has again deteriorated slightly Initial hearing level 82 db final level 50 db residual gap 17 db (at 20 months)

The cause is uncertain There is no justification for further exploration, particularly as her other operated ear remains excellent

(5) A patient whose operation and progress were completely uneventful Initial hearing level 75 db, final level 43 db, residual gap 16 db No special features for comment

Pathology

A careful examination of the site and extent of the disease was made routinely Bellucci (1958) has suggested the following classification

I Early anterior disease with stiffening of the annular ligament normal footplate

II Joint visibly narrowed, focus involves anterior part of footplate, though crura remain free

III The focus involves the joint and more than half of the footplate, the anterior crus is involved

IV Massive otosclerosis a large focus replaces the footplate and the joint, the crura may be adherent to a focus on the edge of the promontory New bone may fill the oval window

The distribution of the current cases between the four groups together with other reported series is given in Table I

TABLE I

All values are given in per cent

Group	Bellucci	Fortmann	Ewert & Shea	This series
I	36	58 (I–II)	9	3
II	41		48	43
III	14	42 (III–IV)	7	37
IV	9		36	17

The high proportion of Bellucci's cases diagnosed in *group I is striking In the* present series only three cases could possibly be placed in this somewhat hypothetical *group and it is felt that* the diagnosis of otosclerosis at such an early stage is difficult Such *limited early disease generally* causes only slight middle ear deafness and exploration accordingly is seldom carried out in this country most patients seen *had already* an obvious degree of [illegible]

[illegible] only after removal of the stapes superstructure enabled an adequate view to be obtained *Indeed* it is submitted that the site and extent of the disease can rarely be *estimated* with accuracy whilst the superstructure is still in position In this *connection Ewert & Shea* draw attention to the high proportion of cases they placed in group IV and attribute it to the fact that reflection of the mucosa *from the* window recess in preparing a

bed for the vein graft often reveals even more extensive disease than would otherwise be suspected. It was interesting to observe that the extent of the lesion was not necessarily related to the age of the patient, the length of the history nor the degree of activity of the disease. It seems probable, however, that the stage of the disease as determined by histological examination of the footplate may be the most important single factor which will influence the final result of surgery in this area.

Complications

(a) facial palsy

A mild palsy occurred once beginning ten days after an uneventful operation in which the nerve was not exposed. It rapidly cleared without treatment and was perhaps due to traction on the chorda tympani.

(b) disturbance of taste

The chorda tympani has been preserved whenever possible. Stretching the nerve is well known to produce taste disturbance but this has never been found particularly troublesome. The nerve was divided in 18 patients. As Guilford (1961) points out, compensation after section of the nerve usually occurs fairly soon. He therefore recommends section whenever the nerve has been stretched or bruised, since in his opinion the paraesthesia which occurs can be permanent. Division of the chorda tympani has also been recommended for easier access to the oval window: this seems unnecessarily destructive, particularly as compensation does sometimes appear to be incomplete.

The nature of this compensation is uncertain. Guilford (1962) uses this term only in respect of clinical improvement and does not infer any regeneration of nerve fibres. There is, however, evidence that true restitution of function can occur. It perhaps occurs when the nerve is simply divided rather than when a segment is excised, for it is difficult to see how alternate pathways can be developed.

(c) vertigo

Most patients experience some vertigo but usually this has completely settled by the second or third day. Unsteadiness has never been troublesome enough to keep the patient in hospital after one week. It is usually more severe in the aged and after an operation on the second ear. Prolonged unsteadiness has never been observed.

(d) re-exploration

As already indicated, re-exploration has been necessary once only, fairly early in the series. It was necessary to readjust the steel pin; the graft was satisfactory and there was no evidence of any intolerance of the middle ear to the foreign material it contained.

(e) otitis media

Otitis media has not occurred. However, as the operation is in a potentially infected area and involves the insertion of a foreign material, it has been a rule to avoid operation if the patient has had a recent cold and to provide an antibiotic cover for seven days. Beales (1962) comments that acute otitis media is not uncommon after the Shea operation, i.e. utilizing a vein graft and polythene strut, and this appears to be borne out by Cawthorne (1962) who experienced it in over 4 per cent of his patients. Although a number of authors have reported this complication, extension of infection to the labyrinth has not been described.

CONCLUSION

The evolution of modern stapes surgery, which began with techniques closely resembling those in use during the last century, has resulted in a number of related methods involving total removal of the stapes.

The short term results of stapedectomy have been shown by several authors to be highly encouraging and this has been confirmed in the present series of 100 consecutive operations in which Schuknecht's technique was employed. Three patients were worse after operation but hearing within 10 db of initial bone conductive level was obtained in 88 of those patients in whom improvement was obtained. For practical purposes the operative result is either excellent or a complete failure. There are few patients between these two extremes. The complete failures are those patients who sustain further hearing impairment; this is usually severe but fortunately it is a very infrequent occurrence.

Although a long period of observation is necessary for final evaluation of the operation, it is felt that the adipose tissue graft and steel pin operation of Schuknecht offers certain technical advantages and in this series was found suitable for all degrees of disease and all types of oval window and incus variation. Provided this operation is carried out with care, it can be done with confidence that the vast majority of patients will achieve a hearing result approximating to their bone conduction level. It is submitted that the results of stapedectomy are so certain that the operation should be the primary treatment of otosclerosis. Indeed, preliminary mobilization can increase the difficulties and at times can increase the dangers; a temporarily successful mobilization undoubtedly predisposes to the occurrence of "floating foot plate".

Increased selection of patients, especially those with very advanced disease, can certainly diminish the number of failures due to cochlear damage but also will result in the exclusion of patients capable of improvement whilst being unsuitable for fenestration. The decision is a difficult one but will probably be solved by further improvements in technical skills and instruments. The operation recently devised by Shea (1963) in which a Teflon piston is inserted through quite a small opening in the oval window region

bed for the vein graft often reveals even more extensive disease than would otherwise be suspected. It was interesting to observe that the extent of the lesion was not necessarily related to the age of the patient, the length of the history nor the degree of activity of the disease. It seems probable, however, that the stage of the disease, as determined by histological examination of the footplate, may be the most important single factor which will influence the final result of surgery in this area.

Complications

(a) facial palsy

A mild palsy occurred once, beginning ten days after an uneventful operation in which the nerve was not exposed. It rapidly cleared without treatment and was perhaps due to traction on the chorda tympani.

(b) disturbance of taste

The chorda tympani has been preserved whenever possible. Stretching the nerve is well known to produce taste disturbance but this has never been found particularly troublesome. The nerve was divided in 18 patients. As Guilford (1961) points out, compensation after section of the nerve usually occurs fairly soon. He therefore recommends section whenever the nerve has been stretched or bruised, since in his opinion the paraesthesia which occurs can be permanent. Division of the chorda tympani has also been recommended for easier access to the oval window; this seems unnecessarily destructive particularly as compensation does sometimes appear to be incomplete.

The nature of this compensation is uncertain. Guilford (1962) uses this term only in respect of clinical improvement and does not infer any regeneration of nerve fibres. There is, however, evidence that true restitution of function can occur. It perhaps occurs when the nerve is simply divided rather than when a segment is excised, for it is difficult to see how alternate pathways can be developed.

(c) vertigo

Most patients experience some vertigo but usually this has completely settled by the second or third day. Unsteadiness has never been troublesome enough to keep the patient in hospital after one week. It is usually more severe in the aged and after an operation on the second ear. Prolonged unsteadiness has never been observed.

(d) re-exploration

As already indicated, re-exploration has been necessary once only, fairly early in the series. It was necessary to readjust the steel pin; the graft was satisfactory and there was no evidence of any intolerance of the middle ear to the foreign material it contained.

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represents a substantial advance in the management of those patients found to have oval window obliteration.

The maximum period of observation of the patients in this series has been three years. It is hoped that the longer term results will be comparable with those of the series reported by Schuknecht *et al.* (1960), in which the author was privileged to take part. The results in those patients continue to be well maintained and any failure occurred soon after operation

Further encouragement is provided by Shea (1961), who found his results after insertion of a vein graft and polythene strut to be well maintained five years after operation. It is beginning to appear hopeful that certain fears expressed about the long-term results and safety of these operations may be unfounded and that in future more attention can be devoted to refinements in technique, particularly in the management of those difficult cases with complete oval window obliteration.

ACKNOWLEDGEMENTS

I wish to express my gratitude to Dr H F Schuknecht who, at the Henry Ford Hospital, Detroit, first stimulated my interest in stapedectomy and under whose guidance I first carried out this form of the operation

These patients were treated in The Royal Infirmary, Edinburgh. I wish to record my thanks to Dr I Simson Hall, in the department under whose charge the series began, and to Dr A Brownlie Smith in the department under whose charge it was completed

I am grateful to them for having entrusted these patients to my care and for having stimulated much interesting discussion I am also indebted to them both for reading the manuscript and making a number of valuable suggestions

ZUSAMMENFASSUNG

Die Erfahrungen und Beschlusse, welche aufgrund einer Serie von 100 aufeinanderfolgenden Stapedektomie-Operationen unter Verwendung einer Fettgewebeverpflanzung und Stahlprothese gezogen wurden, sind beschrieben Achtundachtzig Operationen ergaben eine Luftleitungsschwelle innerhalb 10 db von der praoperativen Knochenleitungsschwelle der Patienten Postoperative Schwierigkeiten und Komplikationen waren minimal Drei Patienten erlitten weiteren Gehorverlust durch die Operation Die Beobachtungsperiode war zwischen einem und drei Jahren Die Methode des Wiederaufbaus wurde in allen Situationen wahrend der Serie als gut befunden Grunde, die zur Bevorzugung dieser Technik fuhrten, sind aufgezeichnet Die Ergebnisse jedoch sind wahrscheinlich unabhangig von der genauen Methode des Wiederaufbaus, welche von den individuellen Chirurgen bevorzugt wird

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POST INTUBATION GRANULOMA OF THE LARYNX

J BERGSTROM
Nykoping Sweden

From the Department of Otolaryngology (Head Karl Rudmark, M D)
Lasarettet Nykoping

Three cases of post intubation granuloma of the larynx are presented and a review of the literature is given The author claims that the lesion of the mucous membrane of the vocal cord which occurs in connection with the insertion of the tracheal tube is essential to the origin of the granuloma A short period of vocal rest should therefore succeed every intubation in order to diminish the risk of the development of a granuloma The treatment of the granuloma should be as conservative as possible Excisions should be carried out with the maximum of caution so that the vocal cord is not damaged

INTRODUCTION

Endotracheal intubation was introduced into anaesthesia by Elsberg in 1910 Since then it has developed into a routine method which is used *in the majority of general anaesthesias* The injuries which may be caused by intubation do not detract from its usefulness There is one exception however, intubation anaesthesia on small children where the risk of laryngeal oedema prevents an unrestricted use (Baron & Kohlmoos 1951) *Meanwhile complications do occur* even though the frequency is low The most discussed of the complications is the post intubation granuloma This should be distinguished from the contact ulcer of the larynx which is also often succeeded by a granuloma This was first described by Jackson in 1928

The contact ulcer is a chronic ulcer located on the vocal process of one or both vocal cords The chief *exciting cause* is the hammering of one cartilaginous vocal process against the other *traumatizing* the thin mucosal covering of both processes The disease usually occurs in incessant talkers or professional voice users It is *found mostly in men* but does occur, though *rarely*, in women It is almost never seen in children

Contact ulcer granuloma is distinguished *from* post intubation granuloma *inter alia* by Holinger & Johnston (1960) and von Leden & Moore (1960) On the other hand New & Devine (1949) *put them together under the same name* contact ulcer granuloma and pointed out the similarity in the basic pathology of the two lesions The difference between the two types of granuloma appears to be in the etiological *factor* (intubation trauma) Furthermore post intubation granulomas are *more common* in women the frequency being about three or four times as great according to Epstein & Winston (1957)

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Coventry Group of Hospitals Coventry England

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Symptomatology

The symptoms of post intubation granulomas are unspecific and correspond entirely to those of contact ulcers discomfort in the larynx hoarseness (which may be slight) or pain extending to the ear and sometimes haemoptysis and a chronic cough (New & Devine 1949)

Diagnosis

Inspection reveals granulomas on one or both sides of the vocal *processes* To begin with these are relatively diffuse but later they become increasingly pedunculated while at the same time paling

Therapy

The non surgical treatment consists of complete vocal rest and the use of antibiotics If seen early enough this treatment may favour regression of the granuloma and complete healing Numerous cases of spontaneous healing have been reported by various authors (Clausen 1932 Brown 1952 *et al*)

Excision of the granuloma may be necessary in order to exclude a malignant tumour Maximum caution should be exercised however, so that the vocal cord is not damaged There is considerably less *risk of recurrence* meanwhile if the excision is delayed until the granuloma has pedunculated (Epstein & Winston 1957)

In other words the literature reveals *that even though etiological differences may exist contact ulcer granulomas and post intubation granulomas are histologically identical They are situated on one or both sides of the vocal cord directly on the vocal processes*

CASE REPORTS

Case 1

A 42 year old woman was admitted after *having taken an* overdose of barbiturates She had been unconscious *in her home for 3* hours On admittance the patient was *cyanotic with rattling* breathing Immediate intubation was done with Magill s *tube no 9* Inspection of the larynx revealed no changes and the *tube filled perfectly* Tracheotomy was carried out 39 hours after intubation *Decannulation* was *possible after a further 86 hours*

6 days after decannulation the *patient* was *hoarse Inspection* revealed that the mucous membrane of the larynx was generally swollen and red, but without any sign *of a granuloma*

10 days after decannulation there was *a pronounced* reddening which was centred upon the edges of the vocal *cord There* was also a tendency to granulation in the posterior parts of the vocal cords and the arytenoid regions

13 days after decannulation *the mucous* membrane of the larynx was paler but granulations were apparent *on both* vocal *cords* There was a tendency to necrosis in the arytenoid *region*

16 days after decannulation the granulations had increased particularly on the left side

Howland & Lewis (1956) found that out of a total of 50 post intubation granulomas three were localized to the anterior 10 to the central and 37 to the posterior part of the vocal cord These conclusions however were not shared by Epstein & Winston who claim that the intubation granulomas are invariably found on the vocal process of the arytenoid

Frequency

The first case of post intubation granuloma was described by Clausen in 1932 Since then numerous authors have submitted single reports but it is nevertheless difficult to obtain a definite opinion on the frequency Howland & Lewis (1956) however claim that granulomas occur in one case per 800 1000 intubations

Etiology

The etiology of contact ulcer granulomas was established as early as 1928 in Jackson s first work In the case of post intubation granulomas however there are many and varied opinions respecting the most significant moment in the development of the granuloma The term post intubation granuloma should imply a trauma in the form of intubation and also a negative examination by a laryngologist some weeks before the symptoms appeared In cases reported it is often unfortunately impossible to find a definite causal connection between the trauma and the granuloma

Pathology

Post intubation granuloma begins with an injury to the vocal cord but the subsequent development is similar to that of contact ulcer granuloma

Barton (1953) summarizes the development after a traumatic scraping of the vocal cord as follows (1) the scraping becomes a (contact) ulcer on account of secondary infection (2) the lesion granulates in order to cover the exposed cartilage (3) the granuloma becomes an inflammatory polyp through central proliferation while the periphery epithelizes

Myerson (1952) describes the difference between a contact ulcer granuloma and a post intubation granuloma as follows

> The granulomatous polyp which follows intratracheal anesthesia is not the same as the granuloma which complicates the well known contact ulcer The latter occurs on the laryngeal aspect of the body of the arytenoid cartilage while the granuloma which is a complication of endotracheal anesthesia is always situated on the same aspect of the vocal process The attachment of the granulomatous polyp gradually changes from sessile to pedunculated whereas the granuloma of the contact ulcer is pedunculated The granulomatous polyp always becomes epithelized and does not occur if removal is performed after epithelization is complete The contact ulcer granuloma recurs when removed it is for this reason that many laryngologists are not in favour of removal of the contact ulcer granuloma but await spontaneous healing

Symptomatology

The symptoms of post intubation granulomas are unspecific and correspond entirely to those of contact ulcers: discomfort in the larynx, hoarseness (which may be slight), or pain extending to the ear and sometimes haemoptysis and a chronic cough (New & Devine, 1949).

Diagnosis

Inspection reveals granulomas on one or both sides of the vocal processes. To begin with these are relatively diffuse, but later they become increasingly pedunculated while at the same time paling.

Therapy

The non-surgical treatment consists of complete vocal rest and the use of antibiotics. If seen early enough this treatment may favour regression of the granuloma and complete healing. Numerous cases of spontaneous healing have been reported by various authors (Clausen, 1932; Brown, 1952; *et al.*).

Excision of the granuloma may be necessary in order to exclude a malignant tumour. Maximum caution should be exercised, however, so that the vocal cord is not damaged. There is considerably less risk of recurrence, meanwhile, if the excision is delayed until the granuloma has pedunculated (Epstein & Winston, 1957).

In other words the literature reveals *that even though etiological differences may exist contact ulcer granulomas and post intubation granulomas are histologically identical. They are situated on one or both sides of the vocal cord directly on the vocal processes.*

CASE REPORTS

Case 1

A 42 year old woman was admitted after having taken an overdose of *barbiturates*. She *had* been unconscious in her home *for 3 hours*. On admittance the patient was cyanotic with rattling breathing. Immediate intubation was done with Magill's tube no. 9. Inspection *of the larynx* revealed no changes and the tube fitted perfectly. Tracheotomy was carried out 39 hours after intubation. Decannulation was possible after a further 96 hours.

6 days after decannulation the *patient* was hoarse. Inspection *revealed that* the mucous *membrane of the* larynx was generally swollen *and red, but* without any *sign of a* granuloma.

10 days after decannulation there was *a pronounced* reddening which was centred upon the edges *of the vocal cord*. There was also a tendency to granulation in the posterior parts of the vocal cords and the arytenoid regions.

13 days after decannulation the mucous *membrane of the* larynx was paler but granulations were *apparent on both* vocal cords. There was a tendency to necrosis in the *arytenoid region*.

16 days after decannulation the granulations had increased, *particularly* on the left side.

19 days after decannulation only a slight hoarseness remained. The larynx was to a great extent free from irritation, but a pea-sized granuloma could be seen on the left vocal process.

24 days after decannulation the granuloma was unchanged and it was removed in its entirety. Histology showed a vascular granulation tissue of an unspecific appearance (Wahlgren).

The subsequent course was normal and a check-up one year later revealed a completely normal condition.

Case 2

The patient was a 53-year-old woman. Intubation anaesthesia was given for 1 hour 55 minutes. Two months later the patient became progressively hoarse and had slight difficulty in breathing. After a further four months examination revealed a pea-sized pedunculated polyp-like formation originating in the vocal cord. This was removed. Histology revealed a granulation tissue polyp (Moberg).

Case 3

The patient was a 56-year-old woman. Intubation anaesthesia was given for about 1 hour. Hoarse almost continually after the operation. After three months granulomas half the size of a hazelnut were found in the posterior commissures on both sides. These were removed and histology revealed chronic purulent inflammation with granulation tissue formations. After four months there was a recurrence in the posterior part of the left vocal cord. Another biopsy revealed the same pathological picture. (Cases 2 and 3 were made available by the Pathological Dept., Sodersjukhuset.)

DISCUSSION

Various opinions have been put forward concerning the moment of greatest significance in the origin of post-intubation granulomas.

The cases described here show considerable variation in the duration of the intubation. The significance of the duration of the tube in the larynx seems to have been overrated. The author (Bergstrom 1962) has previously published material embracing 176 cases of prolonged intubation. Here, despite the prolonged intubation, there was only one case with a granuloma. The necroses which appear in the larynx in connection with prolonged intubation have been put forward as a cause for the granuloma. Bergstrom, Moberg & Orell (1962), however, have pointed out that these necroses are the result of the tube's static pressure and that they are situated principally in the subglottic space. Thus there should be no increased risk to the vocal cord once the tube is in place.

The principal reason for granulomas is probably the epithelial scraping of the vocal cord in connection with the insertion of the tube. This explains why granulomas are more common in women where the membrane of the

vocal cord is only half as thick as men's (Howland & Lewis 1956). There is increased risk of a more extensive and deeper epithelial injury if the tube is inserted through a closed rima glottidis, for example in the event of a laryngeal spasm or when the patient is not properly anaesthetized. The shape of the point of the tube may have some relation to the development of the lesion.

If the tube is correctly placed and of the proper size it is hardly likely that the damage to the vocal cord will increase through moderate movement of the tube or the larynx. Bergstrom's above mentioned work deals with barbiturate intoxicated patients with a relatively prolonged recovery period when the tube remains in place during recurrent swallowing movements. Among these patients only one case of granuloma is recorded.

Granulomas have not been described after bronchoscopy. This is probably because during the procedure the larynx is lifted forward, so that the vocal processes come into another position (Matzker 1953).

In view of the histological similarity between post intubation granulomas and granulomas arising from contact ulcers it seems reasonable to assume that vocal abuse directly after extubation is of some significance and should be avoided during the days following intubation. For the same reason infections of the mouth, nose and sinuses should be treated prophylactically.

In case 3 there was a recurrence after the removal of the granuloma. The risk of recurrence should diminish considerably if the removal of the granuloma is delayed until after it has pedunculated—assuming of course that the patient is not suffering from breathing difficulties.

It is important not to damage the vocal cord during the excision, and the treatment as a whole should be gentle and careful.

ZUSAMMENFASSUNG

Drei Fälle eines Granuloms in *Larynx nach Intubation* werden dargestellt und eine Literaturübersicht gegeben. Der *Verfasser glaubt*, dass die Verletzung der Schleimhaut der Plica vocalis, die beim Einführen des Tubus entsteht, wesentlich für die Entstehung dieser *Granulome ist*.

Ein kurzzeitiges Sprechverbot muss deshalb jeder Intubation folgen, um die Gefahr einer Granulombildung *zu verringern*. Die Behandlung von Granulomen muss möglichst konservativ sein. Eine *eventuelle Exstirpation* soll mit grösster Vorsicht vorgenommen werden, so dass das Stimmband nicht verletzt wird.

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Dept of Otolaryngology
Lasarettet, Nyköping Sweden

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ALLERGIC RHINITIS AND INTRAVASCULAR AGGREGATION OF BLOOD CELLS

SVEN INGELSTEDT and HANS RUNDCRANTZ
Lund, Sweden

From the *Department of Otolaryngology (Head Prof Hj Koch, M D)*
University of Lund

It is well known that intravascular aggregation of blood cells occurs in all sorts of tissue trauma including antigen antibody reaction Judging from the special architecture of the fine vasculature of the nasal mucosa, sludge of blood should readily occur in certain pathological conditions, such as hay fever Dextran of low molecular weight, Rheomacrodex®, has proved an effective inhibition of intravascular aggregation In the present investigation injection of this agent was found to decrease the severity and duration of the reaction of the nasal mucosa to pollen, as measured by the difference in airway resistance The findings suggest that intravascular aggregation in the vascular network in the nasal mucosa may be a component of importance in allergy and infections and if left untreated it may result in pathological changes of the mucosa because of anoxic damage to the tissue

The past decade has witnessed a remarkable and sustained surge of interest in problems bearing on intravascular aggregation of the blood cells Thus in 1950 Thorsen & Hint reported the results of their investigations of the molecular properties of different colloids and the aggregation sedimentation and intravascular aggregation of blood cells Later Gelin and his Swedish group (1956 61) studied intravascular aggregation in diseases with infection and due to trauma such as cold or burns crush injuries or induced hypothermia Observations made on the effect of intravascular aggregation on the microcirculation in animals and in man have enabled the production of preparations capable of inhibiting such aggregation and impairment of the capillary blood flow

Judging from literature studies the anatomy of the fine blood vessels in the nasal mucosa is such as to invite intravascular aggregation in the event of disease

Causal Mechanism of Intravascular Aggregation of Blood Cells

According to Gelin (1956) any traumatic injury to the tissue (fracture contusion burn or cold injury) is followed by intravascular aggregation of blood cells owing to a reduction of the suspension stability of the blood

This investigation was supported by grants from Alfred Österlund's Foundation Sweden

(Fåhraeus 1929). In injured tissue, aggregations of platelets and the formation of white masses soon occur and obstruct the capillaries.

A striking reduction of the flow rate of red cells occurs in the postcapillary venules and *sinusoids with stasis as a result* (Knisley, *Bloch, Eliot* & Warner 1947, Brånemark 1959). Blood is shunted through opened arteriovenous anastomoses and by-passes the occluded capillary bed.

Gelin (1959) gave the following causes of aggregation of blood cells (sludge of blood):

(1) Antigen–antibody reaction.
(2) Conversion of fibrinogen to fibrin.
(3) *Pseudo-agglutination of cells from large and viscidizing* macromolecules such as *fibrinogen*, lipoproteins, gelatin and dextran of high molecular *weight*.
(4) Standstill of blood.

Pathophysiological Effect of Intravascular Aggregation

A number of pathophysiological effects of intravascular aggregation have been observed, such as decreased blood flow in parenchymatous organs as well as in the *periphery (Hinshaw, Pories, Harris, Davis* & Schwartz 1960, Gelin 1961, and others), in reduced oxygen consumption (Löfström 1959), retarded healing of wounds in experimental animals (*Zederfeldt* 1957) and anoxic injury to parenchymatous organs (Lajers & Gelin 1959). It has been stressed in these papers that the poor capillary flow must seriously impair the nutrition of the tissues.

Using a fluorescence microscope, Naumann (1961) studied the circulation in the *nasal mucosa in the rabbit* in association with an antigen–antibody reaction and observed a retardation of the blood flow, stasis, and the formation of white emboli and thrombi.

Intravascular aggregation of blood cells has been considered as a possible pathogenetic factor in certain diseases of the inner ear such as Ménière's disease (*Fowler 1956*).

Macrodex® and Rheomacrodex®

In their pioneer work, Thorsén & Hint (1950) demonstrated that the occurrence or non-occurrence of intravascular *aggregation following infusion* of dextran depended on the size of the molecules. The lowest molecular weight producing aggregation was about 60 000. Dextran of substantially higher molecular weight induced severe aggregation of blood cells and tissue damage in experimental animals. *Infusion* of dextran of low molecular weight, on the *other hand*, was *found not only to inhibit intravascular aggregation* but also to reduce or abolish any existing aggregation.

Two types of dextran solutions are *manufactured* in Sweden: the usual plasma expander Macrodex®, with an average molecular weight of 75 000

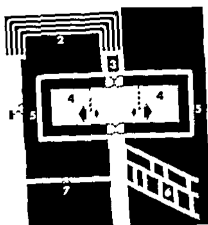


Fig 1 Sketch of the minute vessels of the nasal mucosa 1 Arteriole 2 Capillary network 3 and 5 Postcapillary venules 4 Sinusoid range of possible expansion of filled sinusoid 6 Deep venous plexus 7 Arteriovenous anastomosis

and Rheomacrodex[8], called the flow improver with an average molecular weight of 39 000

In human beings and in animals with intravascular aggregation dextran of low molecular weight has proved (Gelin, 1956, Gronwall 1957, Bernstein & Evans 1960) to

(*a*) increase the peripheral flow three times as much as Macrodex

(*b*) increase the plasma volume by roughly the same extent as Macrodex and Rheomacrodex, besides which it always increases the oxygen availability to the organs investigated ,

(*c*) lower the haematocrit—Macrodex does not

(*d*) reduce the viscosity of the blood—Macrodex does not

(*e*) prevent or break down aggregation by Macrodex of high molecular weight

Dextran has been described as a strong histamine liberator, at least in laboratory animals (Gronwall 1957) but this effect has not been demonstrated in human beings

Remarks on the Physiology and Anatomy of Blood Vessels in the Human Nasal Mucosa

Opinions still differ on various details of the architecture of the blood vessels in the nasal mucosa But judging from the literature, in particular from the publications by Harper (1949) Korner (1937) Messerklinger (1958), Naumann (1960 61) and Swindle (1935), the present conception of the anatomy of the vessels of the mucosa is largely that illustrated in Fig 1

Afferent vessels from the dense subepithelial capillary network empty (*a*) either into large sinusoids (sinusoidal spaces) draining to a deeper venous

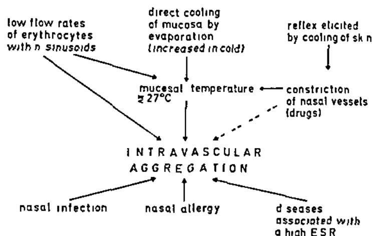


Fig 2 Factors presumably capable of causing intravascular aggregation of blood cells in the human nasal mucosa

plexus, or (*b*) via the postcapillary vessels, directly into the deep plexus The sinusoids give the tissue a cavernous appearance, above all in the mucosa of the inferior and middle conchae and in some parts of the septum

This peculiar architecture of the vascular system explains the wide range of variation of the blood flow through the nasal mucosa and corresponding change consequent in its colour and temperature The degree of swelling of the mucosa is also under the control of the vasomotor nervous system It is believed that the main purpose of the extremely dense network of the nasal mucosal blood vessels, and their ability to vary their calibre within very wide limits, is to humidify and warm inspired air The vasomotor reactions in the nose are readily affected by local stimuli such as physical changes in the inspired air trauma, infections allergy, and drugs The reaction is also influenced by systemic factors such as endocrine and nervous disorders and vessel reflexes in response to cutaneous thermal irritation Factors known or believed to affect the blood flow in the human nasal mucosa are illustrated in Fig 2

A perusal of the literature failed to reveal any investigation of the possibility of intravascular aggregation in the nasal mucosa being a factor of importance in diseases of the nasal mucosa in man

Purpose of the Investigation

The purpose of the investigation was to ascertain whether intravascular aggregation of the blood cells in the nasal mucosa could be demonstrated in patients with allergic rhinitis If such aggregation occurred it should presumably be possible to counteract it by Rheomacrodex

The problem could be approached by comparing the nasal airway resistance in patients with hay fever

(*a*) before and after instillation of pollen extract only,

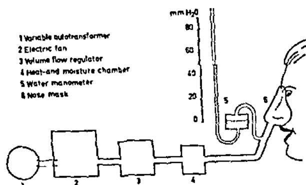


Fig 3 Apparatus for the measurement of airway resistance in the nasal cavities

(*b*) before and after identical provocation immediately after infusion of Rheomacrodex (dextran of low molecular weight),
(*c*) same provocation after infusion of Macrodex

Measurement of Airway Resistance in Nasal Cavities

Determination of the airway resistance requires continuous measurement of the air flow velocity and of the trans airway pressure drop ' The principles of the procedure are well known from studies on mechanics of breathing A special apparatus was designed (Allander & Ingelstedt) with a volume flow regulator which delivers an absolutely constant flow of air even on variation of the resistance between 0 and 9 cm H_2O The air current is delivered by a fan and is heated to 35°C and is saturated with water vapour in a heat moisture chamber The air flow rate used was 20 l/min A rubber mask connected to the apparatus was fixed air tight over the nose without any compression of the nostrils The constant air current was forced through the nasal cavities of the patient who was instructed to hold his breath during the recording period and to keep his mouth open and the soft plate relaxed

The nose mask is connected to one end of a water manometer, the other end of which is exposed to the atmosphere The air pressure in the mask thus reflects the airway resistance offered by the nasal cavities to the constant air flow used (Fig 3)

Experimental Design

The experiments were performed only during the non pollen season on volunteers known to have hay fever

In order to avoid any overlapping of the effects of consecutive tests, all experiments on a given volunteer were carried out at an interval of at least 4 days The dose of pollen extract necessary to produce a marked reaction and nasal occlusion was assessed by a series of pre tests with increasing amounts of the pollen The dose used in the individual tests was never so

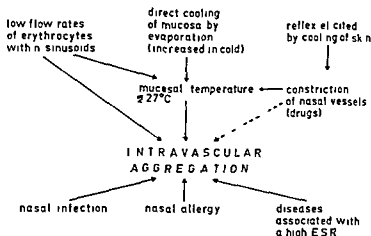


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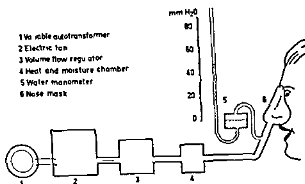


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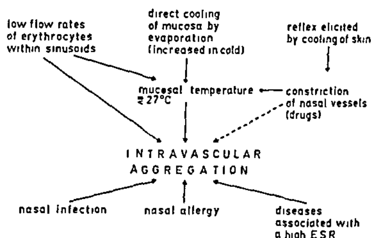


Fig. 2. Factors presumably capable of causing intravascular aggregation of blood cells in the human nasal mucosa.

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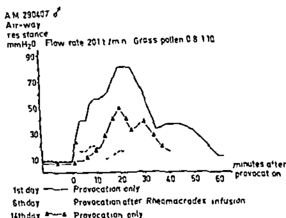


Fig 7

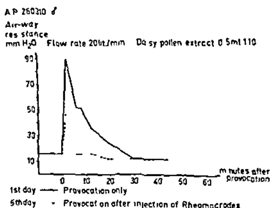


Fig 8

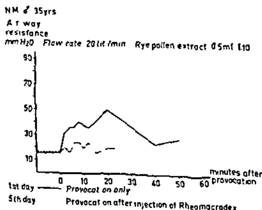


Fig 9

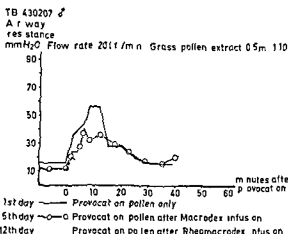


Fig 4

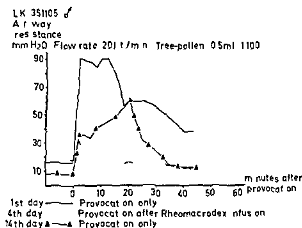


Fig 5

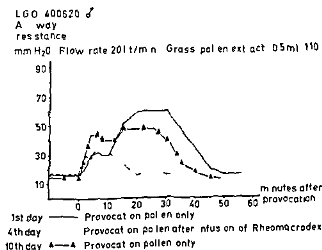


Fig 6

other investigators to counteract intravascular aggregation, suggests that such aggregation may be a component or an accompaniment of the acute allergic reaction of the mucosa. Intravascular aggregation cannot, of course, be proved without direct inspection of the vessels.

Naumann's (1961) investigation of the allergic reaction of the mucosa in the rabbit in which intravascular aggregation was demonstrated, lends support to our assumption.

As pointed out by other investigators referred to above, untreated intravascular aggregation may result in anoxic lesions in the tissue involved. In chronic allergy of the nasal mucosa prolonged intravascular aggregation in the mucosa might contribute to the development of mucosal hyperplasia, polyposis etc. Impaired nutrition of the tissues because of long standing intravascular aggregation might be an important factor in the causation of such conditions. Like allergy, infections might also give rise to aggregation of blood cells in the fine blood vessels. It would appear that the problem warrants further investigation.

ZUSAMMENFASSUNG

Intravasale Aggregationen der Blutkörperchen kommen bekanntlich bei jeder Art von Gewebsschaden einschliesslich Antigen-Antikörperreaktionen vor. Ausgehend von dem speziellen Aufbau des feinen Gefässnetzes der Nasenschleimhaut, wird vermutet, dass eine Aggregation der Blutkörperchen bei gewissen pathologischen Zuständen, so auch der allergischen Rhinitis, vorkommen können.

Es konnte gezeigt werden, dass Dextran (Rheomacrodex) mit einem niedrigen Molekulgewicht eine effektive Hemmung der intravasalen Aggregation hervorruft. Die Untersuchung hat ergeben, dass es mit Hilfe von Rheomacrodex möglich ist, die Stärke und Dauer der Nasenschleimhautreaktion gegenüber Pollen, gemessen durch den Unterschied des Luftwiderstands, herabzusetzen.

Die Ergebnisse lassen die Vermutung zu, dass eine intravasale Aggregation in dem Gefässnetz der Nasenschleimhaut bei Allergien und Infektionen ein Komponent von Bedeutung ist, der, wenn er unbehandelt verbleibt, auf Grund anoxischer Gewebsschaden pathologische Veränderungen der Schleimhaut hervorrufen kann.

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heavy as to produce complete occlusion which would make it impossible to measure the airway resistance.

The titrated dose was then given and the airway resistance measured. The test was repeated later but this time after infusion of 10 % Rheomacrodex in a dose of 1 g/kg body weight and in some cases later after infusion of a similar dose of Macrodex. The series of tests was always concluded with provocation by the pollen extract only. Each test was performed with the dose titrated by the pre-tests and with extract from the same bottle as that used for the titration of the dose. The volume to be instilled was carefully measured in a finely graduated pipette and was sprayed in equal amounts into each nasal cavity. The tip of the spray had side holes but no end hole. It could be readily inserted into the nasal cavity. In order to avoid aspiration of the antigen the patient was requested to hold his breath while the solution was being sprayed. This technique enables direct application of the entire dose to the mucosa of the nasal cavity and to the mucosa only.

The airway resistance was determined at the beginning of each test; this required only about 15 seconds. The pollen extract was then sprayed into the nasal cavities for about 2 minutes (each cavity 1 minute). After an interval of 2 minutes the patient was requested to blow his nose. The airway resistance was measured every second to fifth minute for altogether 30 to 60 minutes. The patient was requested to blow his nose thoroughly because any residual accumulation of secretion would substantially increase the airway resistance.

MATERIAL AND RESULTS

The investigation was carried out on nine volunteers with known but untreated pollen allergic rhinitis. The findings, which were essentially the same in all the volunteers, are exemplified in Figs. 4–10. It is clear from the illustrations that the increase in the airway resistance was roughly equal on both occasions after instillation of pollen only, and that pre-treatment with Rheomacrodex invariably reduced the severity and duration of the reaction to the antigen. It is also apparent that Macrodex had no such effect.

DISCUSSION

A regular observation in the present investigation was that the second instillation of pollen from the same bottle produced a somewhat weaker reaction than the first instillation of pollen from the same bottle. This may be explained by the fact that during storage pollen extract loses part of its antigenic activity (Hjorth 1957). A similar decrease was also noticed in the reaction to Macrodex only, probably for the same reason.

The marked decrease in the severity of the reaction of the nasal mucosa to pollen extract after infusion of Rheomacrodex, which has been shown by

RECURRING MIDDLE EAR INFECTIONS AND SERUM PROTEINS IN INFANTS

U K Kivimanta
Helsinki, Finland

From the Helsinki University Central Hospital E N T Clinic (Head Prof U Siirala M D), Helsinki

The causes and therapy of the recurrent otitides in infants are reviewed, special attention being paid to the correlations between gamma globulin and infectious diseases The present material consists of 18 consecutive cases of recurrent otitis Hypogamma globulinemia is considered as a dominating factor in these cases Gamma globulin administration is indicative of better curative results

Etiology of Ear Infections in Children

Middle ear infections are among the most common illnesses afflicting children particularly those under two years of age Some children s clinics are finding ear infections in nearly one third of the patients The disease is more common in children than in adults There may be several reasons for this

1 Various contagious diseases of children exhibit upper respiratory symptoms

2 Immunity has developed poorly in children Consequently these children s diseases as well as the common cold infections are apt to be complicated

3 The Eustachian tube is short and wide in children and infection can therefore easily reach the ears from the nasopharynx Bottle feeding may mechanically promote ear infections The breast fed child is usually in a semi sitting position When bottle fed however the child as a rule is lying in a recumbent position to allow the milk to flow through the rubber cap into the nasopharynx In ear operations of bottle fed babies milk is often encountered in the middle ear Postmortems of children having succumbed to pneumonia show middle ear infection in 90 per cent even if no symptoms indicative of this were noted during life

4 Infantile lymph tissue is in a stage of active growth I have gone over a series of 8000 cases of my personal tonsillectomy and/or adenoidectomy material and found that children quite often exhibit symptoms of the pharyngeal lymph tissue in the first year of life, sometimes even from birth The peak of symptoms occurs in the fourth year although surgery for the troubles is most often done at the age of six just before the child starts going to school

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E. N. T. Department, University of Lund, Sweden

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slight pressure can be applied to make the drug reach the middle ear and tube

2 *Poor home environment recurrence of illness from encompassement and inadequate diet* It is known that the ears of a child from poor home surroundings or from a day nursery or children s institution dry up with hospital care but begin to drain soon after returning to the former milieu The reason for the poor results may partly be the omission of home treatment

With sulphonamide and antibiotic therapy mastoidectomies in the western countries all but vanished Within recent years however a regression seems to have occurred in this respect Not only apparent mastoiditis but also the masked or latent type seems to have increased This may stem to a certain degree from too short a period of antibiotic therapy or too low a concentration of medication This is particularly so with an insufficient dosage of sulphonamides which can lead to a watering down of the infection It may also be due to new causative microorganisms as concluded from the frequency of their incidence Two decades ago hemolytic streptococcus alone often caused as much acute otitis as all the other bacteria together Penicillin has apparently eradicated streptococci so effectively and checked staphylococci so poorly that the latter are according to Birrel (1960) today the most important bacteria and they present themselves as penicillin resistant Finnish contributions have not shown that staphylococci play such a significant role in otitis (Lahikainen 1953 Vuori 1959) Viral infections have increased at least relatively perhaps as a result of antibiotic therapy (Lagle 1946) In all probability antibiotics even when properly used are partially responsible for the recurrence of ear infections since they eradicate the germs so rapidly that the patient is not given time to develop antibodies

Gamma Globulin

Gamma globulin contains 98 per cent of the antibodies (Cohn *et al* 1944) Its amount reflects immunobiological responses A marked increase in the gamma fraction in various diseases justifies making some conclusions about the reactivity of the body However no conclusions can be drawn from the gamma globulin amount concerning the level of the antibody titer and the hyperergic reaction readiness in inflammatory diseases (Dittmer 1961 *a*)

Of the plasma proteins the albumins are entirely and the globulins are 80 per cent synthesized in the liver The liver is able to repair 25 per cent of the circulatory plasma protein the regeneration of albumin being 0 7 + 0 93 per cent a day (Miller *et al* 1951) Gamma globulin is formed in the R E tissue of the liver and outside of it Lymphatic cells—lymphocytes plasma cells and possibly macrophages—form gamma globulin and above all antibodies The plasma cell very likely originates from the reticuloendothelial cell (Kolouch & Cambell 1947) In the adult blood stream approximately 25 g of gamma globulin circulates (Domz & Dickson 1957) The

Because of its magnitude lymphatic tissue can interfere with the movement of the palate and with the closing of the Eustachian tube. Since the tonsils are often infected and enlarged tonsils in addition frequently cause paranasal sinus inflammation, the spreading of ear infections in children can be understood.

5. The middle ear of children often contains residual myxomatous connective tissue left over from the fetal stage. This tissue is said to serve as a culture medium for pathogenic organisms. Ruedi (1952) states that children with this condition are especially prone to middle ear infections and the infections in turn prevent the regression of this tissue which would otherwise occur in the first or second year of life.

6. Allergic rhinitis is claimed to be the causative agent of recurring otitis in about 10 per cent of children (Suchs 1952). Lundborg (1955) considers, as I do, that this number is too great.

Otology has become separated from general surgery in Europe during the last hundred years and in Finland during the last fifty years. This may be one reason why the treatment for ear infections up to the World War II was substantially surgical. For restoration of the function of the Eustachian tube and for eradication of the infective focus the disranged pharyngeal lymph tissue was removed by surgery. Paranasal sinus infections were treated either conservatively or operatively. These measures often resulted in curing the ear, but frequently surgery of the ear had to be resorted to. The number of ear infections requiring surgery was decimated by the introduction of sulphonamides and particularly by antibiotics. The effect of these drugs has been so apparent, and they have been so efficiently advertised and promoted that few physicians have had the courage to attempt to treat an ear infection without their use.

Interference with Recovery

Not all infected ears respond to these drugs or to surgical treatment. The reasons may be as follows:

1. *Incorrect drug or inadequate duration of therapy.* At present penicillin is still the drug of choice in ear infections. If the patient does not tolerate it or if antibiotic sensitivity tests indicate that it is completely ineffective, resort should be made to sulphonamides, streptomycin or wide spectrum antibiotics. The drug must be given in full dosage until the ear is dry, the eardrum appears completely quiescent and hearing has returned to normal. If the eardrum has not perforated due to otitis, a week's antibiotic therapy is generally considered sufficient. In this era of antibiotics otologists are not everywhere as unanimous concerning the necessity or usefulness of paracentesis (myringotomy) as they are in Finland. If the eardrum has perforated, ten days of treatment is recommended. If symptoms are then still present, the therapy should be continued for a longer period of time. In scantily draining otitis with a large perforation an antibiotic applied locally, perhaps combined with cortisone, may be effective. If the perforation is

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physiological fluctuation of the gamma-globulin content in healthy adults ranges, according to Dittmer (1961 *b*), from 13 0 to 18 0, averaging 16 1 relative per cent of total proteins According to Barkve (1958) it averages 18 6, and according to Oberman *et al* (1956) 17 91 ± 1 477 relative per cent

Agammaglobulinemia

The Swiss Loffler (1951) described a case of recurring pneumococcic meningitis with a total lack of blood gamma-globulin where the meningitis was repeatedly cured by antibiotics Almost all the papers considering agammaglobulinemia, however, begin with the mention of an American *Bruton In 1952 he described the syndrome of* agammaglobulinemia in an eight-year-old boy who had had several serious infections, including middle ear infections When the boy was given 3 2 g or 20 ml of a 16 per cent gamma globulin suspension once monthly he remained well for a year When the pattern of the disease was recognized agammaglobulinemia could be diagnosed afterwards from several blood samples preserved and stored in the laboratories prior to the discovery of the syndrome

Total agammaglobulinemia hardly exists at all Perhaps it would be more correct to speak of hypogammaglobulinemia, for in paper electrophoresis albumin always marks gamma globulin, and in cases where no gamma globulin is detected by the conventional Antweiler electrophoresis a small amount of gamma globulin may always be found by immunoelectrophoresis *However, the amount detected in this way may not* exceed 0 15 g per 100 ml Wallenborn (1960), who related nearly all the clinical communications published to that date and described two cases of his own, diagnosed what he called agammaglobulinemia in a four year old otitis patient whose gamma globulin was 6 9 per cent In a two volume monograph on plasma protein, Putnam (1960 *a*) registers as *hypogammaglobulinemia* cases with a gamma globulin content decreased to one half or one third of normal However, partial immunity weakness in antibody development may exist when the gamma globulin amount presents no changes

A or hypogammaglobulinemia

This typified by

1 Susceptibility to bacterial infections often exists from childhood on Foremost among these diseases are found respiratory infections such as sinusitis, middle ear infections, pneumonia, as well as meningitis and bacteriemia *It is not necessary for the infections to be more severe than those in* other people and they usually respond to chemotherapeutics and antibiotics (Hayles, 1956) This is evidently the reason why the disease entity was not discovered before the antibiotic era The patient obviously did not live long enough without antibiotics to have a history of recurring infections

The patients seem to escape virus infections Often they do not exhibit a greater number or more severe cases of measles, mumps chickenpox or

polio than normal human beings (Hayles). Smallpox virus is an exception to this. Several cases of vaccinia gangraenosa seu generalisata in patients with agammaglobulinemia have been described. On the other hand it should be noted that many an agammaglobulinemic child has been vaccinated against smallpox without complications.

2. Circulating gamma globulin is decreased. The other serum protein fractions are normal.

3. There is partial or complete lack of antibodies circulating in the blood. Thus successful homotransplantations of the skin have been done in unrelated children with congenital agammaglobulinemia. The phenomenon is often called immunological paralysis (Felton & Ottinger 1952, Varco *et al* 1955). The isohemagglutinins are absent in cases of agammaglobulinemia. This means that a patient belonging to groups O, A or B has low anti-A or anti-B titers, or that these characteristics are missing entirely. In the AB group we cannot decide whether agglutinins are absent or not.

4. The immunologic condition is influenced very little by active immunization. Serologically demonstrable antibodies are not produced by bacterial vaccination. The Schick test remains positive regardless of the administration of diphtheria antitoxin. Yet cases of agammaglobulinemia have been described where the resistance to bacteria appears normal.

Varieties of a- or hypogammaglobulinemia

The disease can be classified as follows:

1. Congenital, present in boys right from birth, thus a recessive genetic defect related to sex, which appears in one half of the boys whose mother carries the gene, even though she herself is clinically well in regard to infections. The congenital form phenotypes in both the identical twins (Molander 1958). Approximately 150 cases have been published (Good *et al* 1960), the first one in Finland in 1961 (Janner *et al* 1961). Reticuloendothelial hyperplasia is typical of these cases. Enlargement of lymph nodes, liver and pancreas is often seen, with occasionally hypertrophy of the spleen in connection with hemolytic anemia, leukopenia and thrombocytopenia. In biopsy of marrow and lymph tissue the plasma cells are decreased. Roentgenologically typical widespread lung parenchyma diseases are seen, in which paradoxically hilar gland hypertrophy is not present. The pharyngeal lymph tissue is poorly developed despite recurring respiratory infections.

2. Acquired hypogammaglobulinemia is a secondary disease of the lymphatic and reticular systems. It is found in all age groups and in both sexes. Hypertrophy of the lymph nodes and spleen together with leukopenia are also demonstrable in the acquired form. The cause is unknown. Splenectomy may result in a cure.

3. Physiologic transitory hypogammaglobulinemia may occur in children shortly after birth. Newborns have originally the same gamma globulin level as adults, sometimes even higher. Shortly after birth the gamma globulin

level falls exponentially with about a 20 day half life The decrease is about one-third of the normal level during the first month of life and stays there for about three months, followed by regular and slow rise reaching the adult level at 6–8 months of age (Wallenborn, 1960), *or, according to other sources,* at one year of age (Moore *et al* , 1949), or 5–7 years of age (Putnam, 1960) The *most reliable statisticomathematically treated* normal serum protein values of healthy individuals are to be found in Oberman *et al* (1956)

4 Secondary *hypogammaglobulinemia* Young children's dysproteinemia exhibits a radical fall of serum-protein fractions, fibrinogen excluded The pediatric type of dyscrasia differs from primary agammaglobulinemia, either congenital or acquired, in that the susceptibility to infections is not increased There are plasma cells in the marrow, and antibodies are produced Possibly one or several grave infections are able to paralyze the body's capacity to form gamma globulin (Lundström, 1955) A mild hypogamma globulinemia, even occurring *during the second year of life, does not* always imply true dysproteinemia, Dittmer (1961 *c*) suggests

Several studies show *that* a six week-*old child* is already *capable producing* antibodies It is possible that some children, having primarily appreciable quantities of antibodies traced to the mother, may develop less antibodies (Batson *et al* , 1958, Thrupp, 1958) Recent viral studies, however, indicate that a child reacts from birth quickly with the production of antibodies, regardless of age or birth weight The homological antibodies inherited from the mother do not appear to interfere with active antibody formation (Eichenwald & Kotsevalov, 1960) Dittmer (1961 *c*) has noted gamma globulin rises to 30 per cent in the course of the first three months of life Accordingly, he doubts the R-E immaturity of neonatal life

Gamma Globulin Therapy—Indications

Gamma globulin has a prophylactic use even in people presenting no blood inadequacies By giving approximately 30 per cent of the dosage needed *for complete protection,* a *milder so called mitigated or abortive* form of illness develops, and as far as is known, permanent immunity results *It has* been used *especially* in measles *for infants of* six *months to* three years old, as well as in infectious hepatitis, rubella, pertussis and polio In the latter protection is expected *for 2–5 weeks following administra* tion In addition it has been used in the toxic form of scarlet fever and also in preventing orchitis due to parotitis In the latter gamma *globulin should be* given during the first day of illness In measles encephalitis gamma globulin may give relief

After a and hypogammaglobulinemia were established it was found that some children s infections were resistant to antibiotics but when the drugs were given together with gamma globulin, excellent results were obtained Animal experimentation confirms these practical results *It has* provided evidence that human gamma globulin protects an animal from the conse-

quences of otherwise fatal bacterial inoculation (Zimmerman 1960) Numerous human cases have shown an otherwise ineffective wide spectrum antibiotic becoming effective when given in combination with gamma globulin (Schonholtz *et al* 1957) In a patient with normal gamma globulin content who had serious therapy resistant infections gamma globulin apparently led to recovery (Barandum *et al* 1959) In infants who often have bacterial infections resistant to antibiotics gamma globulin given with antibiotics leads to rapid recovery (Harris & Schick 1954) The number of nosocomial infections in children can in all probability be decreased with gamma globulin treatment (Lundstrom 1955) Contrary results have been obtained by some investigators in double blind experiments where it has been impossible to prove the effectiveness of gamma globulin in curing children with acute infections In 13 to 24 month old children the incidence of infection increased with the rising gamma globulin level Accordingly the gamma globulin rise following an infection in young children could reflect poor antibody formation This difference is not exhibited in children under 12 months of age (Finkel & Haworth 1960)

Antibiotics are effective in patients with agammaglobulinemia With antibiotic prophylaxis an attempt can be made to prevent infections but the results with both penicillin and wide spectrum drugs are not encouraging (Lundstrom) Preventive vaccination may be hopeless since antibody formation cannot be expected At the present time human pooled gamma globulin is commonly used It contains viral antibodies also Antibiotics in combination with preserved gamma globulin have proven very useful in hypogammaglobulinemia Gamma globulin administration to premature infants is considered by some to be clearly protective against nosocomial infections (Wasz Hockert 1962) while prophylactic use is claimed by others to be ineffective (Dahl 1959)

Encouraging results have been obtained in the staphylococcus streptococcus pneumococcus pseudomonas proteus and *E coli* infections If gamma globulin therapy is combined with wide spectrum antibiotic treatment the effect of the latter will be multiplied (Gitlin & Janeway 1956) Even if cured by this combination of therapy such bacterial diseases have not been connected with quantitative hypogammaglobulinemia (Lundstrom)

Diamant *et al* (1961) studied the effect of gamma globulin therapy on the recurrence of acute otitis not taking the serum protein levels into consideration Otitic children born on odd dates underwent paracentesis and were given *0 6 ml* per kg of 12 per cent gamma globulin once a month In children born on even dates paracentesis was done but no gamma globulin was given Both the series contained about 100 children In the children receiving prophylactic gamma globulin the otitis relapse incidence amounted within 15 months to *merely half of* that in children with no prophylaxis Among those not receiving gamma globulin fivefold relapses occurred whilst among those receiving gamma globulin there were no more than twofold relapses Both of these differences were statistically significant

Gamma globulin is effective only in diseases against which it contains antibodies. People receiving gamma globulin suffer from the usual respiratory infections as normal ones do. Similarly, gamma globulin and antibiotics are not able to restore extensive anatomical changes such as occur in chronic ear or sinus infections. Those cases require the time-honoured surgical treatment.

Gamma globulin dosage

This is based on three facts.

1. The half-life of intramuscular gamma globulin shots varies from 13 to 32 days (Wallenborn). In an agammaglobulinemic patient the circulating time of injected gamma globulin equals that of a healthy individual. This indicates that the illness is due rather to a lack of synthesis than to an increased destruction. This has been demonstrated, for instance, by radioiodinated gamma globulin (Owen *et al.* 1958).

2. Gamma globulin is a heterogeneous substance. It contains several antibodies with degradation rates ranging from 17 to 58 days (Martin *et al.* 1957).

3. 100 to 150 mg of gamma globulin per 100 ml of serum or approximately 2 per cent of total serum proteins appears to be the minimum required in preventing infections. This level is achieved by injecting 0.1 g per kg of body weight or approximately 1 ml per kg of a 15 per cent preparation. This dosage is usually given for prophylaxis against infection. The smallest dosage has been 15 mg per kg or 0.02 ml per kg used prophylactically in infectious hepatitis. Refrigerated gamma globulin maintains its effectiveness for years. When administered, its effective half-life is estimated to be three weeks.

Disadvantages of gamma globulin treatment

1. Large quantities and frequent injections are necessary.

2. It is expensive. One phial of 2 ml 15 per cent gamma globulin costs about U.S. $3 in Finland.

3. Only passive immunity results.

4. Patients generally tolerate 10–20 ml administrations of gamma globulin given thrice a week over an extended period of time, but occasionally doses of over 20 ml may produce chills, fever and muscular weakness. A rise of temperature usually occurs 6 hours following injection in patients who are in the acute stage of the illness (Lundstrom).

5. Prophylactic antibiotic therapy is often necessary in addition to gamma globulin.

True contraindications have so far not been reported. It is argued that no allergy should develop since the protein is of human origin.

Alteration in the Serum Protein Pattern due to Inflammatory Diseases

Changes in the albumin/globulin ratios are caused by most of the illnesses but the amounts of albumin are nearly always decreased and those of globulin increased During the acute phase of bacterial diseases the albumin drops alpha fraction goes up and fibrinogen rises The gamma fraction elevation takes place somewhat later than other changes most often during the second week and the maximum is reached earliest in the third week The increase is often observed only when the fever has been present for at least a week *An apparent parallelism between the rise of gamma globulin and serologically* determinable antibodies has not been proven

If the reticuloendothelial system is affected by a viral infection as in hepatitis mononucleosis or toxoplasmosis gamma globulin will increase early the maximum often being reached in the first or second week regardless of the fever or the alpha globulin rise In such cases the elevation of gamma globulin is also protracted whereas after an acute bacterial infection alpha and gamma globulins return to normal almost simultaneously as does albumin (Belfrage 1958)

A rising gamma globulin reading detected by repeated check ups is a prognostically favorable sign in chronic inflammatory processes in adults The clinical remission of an inflammatory disease is liable to induce a slight gamma globulin rise (Dittmer 1961*c*) A child with occasionally recurring common infections generally seems to have a mild hypergammaglobulinemia although a low rating would be expected as a hint of a defective reaction ability (Dittmer 1961*c*) Alpha and beta globulin values are elevated in nearly all acute diseases an exception being made only by the infections of the ear especially chronic ones where the values may decline Dittmer (1961*c*) reports without revealing the sources of his knowledge

In small children with common cold and infectious suppurative diseases (nas pharyngeal infections sore throats acute and chronic otitis media bronchitis pneumonia) alpha globulin increases and even beta globulin secondarily A heavy gamma globulin reaction is seldom met with but once it occurs it is prognostically significant in the same manner as in older children Extremely high gamma globulin values at the onset of the illness indicate a serious *general disease and its further rise during the* continuance of the illness seems to be an infaust sign (Dittmer 1961*d*) Chronic infections show a higher gamma globulin rise than would be expected due to specific antibodies because the latter constitute only an insignificant amount of total gamma globulins

Suirala & Vuori (1954) investigated the effect of acute otitis on the serum proteins and later on (1959) further investigations were carried out by Vuori for his doctoral dissertation on the basis of 82 patients These studies have confirmed that the average serum protein pattern presenting in acute and chronic bacterial suppurative otitides differs from that of normal serum in the same manner as do other acute inflammatory diseases

Present Material

In the Helsinki University Central Hospital ENT Clinic and at its Out Patient Department the staff has been put to the touchstone by the recurrent otitides in children Despite antibiotic therapy given *lege artis* and regardless of excellent home care and adequate nutrition including additional vitamins some of the children are unable to lose their susceptibility and periodically return to the Out Patient Department up to 10 to 15 times a year for paracentesis or because of relapsing otitic discharge After every possible means has been tried the child is hospitalized He may have been hospitalized repeatedly up to ten times a year He is examined thoroughly he receives strict local and general treatment daily and seems to recover but he falls ill again after a week or a fortnight

The present study is based on 18 consecutive cases of this kind admitted to the children s ward in 1961 eight of these being girls and ten boys Ear troubles had begun in six of them 0 to 2 months after birth (in four at 2 months of age) in five at 3 to 6 months in four at 7 to 12 months and in three at 13 to 24 months of age (If the past history were most minutely taken the debut of illness would concentrate still more around the three months of age The material gathered after these 18 cases implies this at least)

According to the history all the children had received some kind of immunization nearly all to BCG vaccine to pertussis diphtheria and often to polio and smallpox (Barandum *et al* consider vaccination as a possible cause of transitory protracted antibody deficiency in infants with no reciprocal loan immunity) There was no mention of any complications from immunization Some of the children have been affected with measles or rubella and a few with chickenpox While hospitalized during an endemic chickenpox a few children fell ill with it Special attention is drawn to the fact that at least one child became ill with measles at age of two months The course of these illnesses was otherwise uneventful

Clinical Examinations and Earlier Measures

It is sometimes difficult to decide whether the size of the adenoid in one to two year old children is exceeding its physiological limits In middle ear infections it may also be difficult to decide whether the adenoid is primarily or secondarily infected

Little interest was taken in the surgical removal of the adenoid Firstly the patient s small stature was shunned and secondly some are inclined to see a correlation between adenoid tissue and antibody formation Even in cases in my material where the adenoids were removed it was done with extreme reluctance *um etwas zu tun* all other means having already been tried in vain Adenoids were removed from nine Prior to the surgery the ears had drained for 7 to 24 months The youngest adenoidectomy child was 9 months old seven children underwent surgery at the age from 1½ to



2 years The adenoids removed were classified as small or not over medium size The adenoids of the unoperated children were examined roentgenologically None was considered to be large Four children were stated to have no adenoids Tonsils had been removed from only one patient The tonsils in all the others were considered either small or middle sized and pale

The general X ray thorax finding was negative Often however the bronchial configuration appeared more pronounced the hilum remaining within normal limits The lung changes in two children were initially elsewhere interpreted as tuberculotic but check ups could not confirm this suspicion

A boy who had undergone a monthly bilateral myringotomy since he was 6 months old underwent surgery at 2½ years of age for a suspected mediastinal tumor Both the surgical finding and biopsy resulted in a diagnosis of hyperplasia thymi A roentgenologist not directly involved in this study has in three of ten thorax records additionally mentioned the thymus obviously is voluminous The establishment of benign thymoma and thymus hyperplasia as a coagent of agammaglobulinemia dates from 1953 In all probability this initiates a new era in science and the clinic (McLean *et al* 1957 Miller 1961)

In two cases X ray showed shadowing of the paranasal sinuses One of these was examined for gamma globulin while the patient underwent maxillary irrigations He had the highest gamma globulin value in the series 11 7 per cent The maxillary sinuses of the other case were healed by irrigations 12 days before electrophoresis He had the second highest gamma globulin rate in the series 11 5 per cent It is known that the sinus infections will result in elevation of gamma globulin in normal patients (Palva *et al* 1962)

X ray examination of the mastoids revealed a slightly veiled cellular system in which the normal sized atticus and auditory ossicles were distinguishable Unilateral mastoidectomy was performed on four infants The operative finding in all of these was a normal sized antrum and atticus a pneumatization corresponding to the age with a thickened mucous membrane and purulent secretion The biopsy was otitis media subacuta seu chronica

During the hospital stay the children s blood samples were taken The red blood count presented nothing unusual It is noteworthy that no anemia occurred About the time of admission the sedimentation rate and leucocytic count were often elevated but the rates returned to normal in a week or a fortnight Differentiations exhibited similar changes which for example Koskinen (1938) reported in his doctoral dissertation on middle ear infections Accordingly a neutrophilic combat phase and a lymphocytic recovery phase were often to be discerned Blood eosinophilia exceeding 5 per cent did not occur

Bacterial cultures were taken either through an imperforated eardrum by myringotomy or puncture and aspiration or which was more usual from a

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TABLE 1

Characteristics	Total protein	Albumin	Alpha₁ globulin	Alpha₂ globulin	Beta globulin	Gamma globulin
Age under one year						
Number = 3						
Mean	7 00	64 67	4 37	11.33	9 77	9 40
Average error	0 115	2 22	0 80	0 54	0 91	1 07
Age one to two years						
Number = 12						
Mean	7 59	65 46	4 41	10 44	10 42	9 22
Average error	0 26	1 93	0 40	0 86	0 52	0 44
Age over three years						
Number 3						
Mean	7 53	61 13	4 33	12 77	11 43	10 30
Average error	0 34	1 52	0 19	1 03	0 85	0 94
t tests The rates of Oberman and co workers contra present material						
Age under one year						
n + n 18						
Diff of means	0 32	+12 77	−1 29	−2 52	−6 31	3 17
Its mean	0 162	2 54	0 846	0 734	1 14	1 21
t	1 98	5 03	1 52	3 43	5 55	2 62
P		0 001		0 01	0 001	0 01
Age one to two years						
n + n 32						
Diff of means	0 67	+10 77	0 52	2 02	−3 90	−4 38
Its mean	0 285	2 54	0 45	1 02	0 87	0 845
t	2 35	4 24	1 16	1 98	4 48	5 18
P	0 05	0 001			0 001	0 001
Age over three years						
n + n 18						
Diff of means	0 42	+10 31	0 74	+0 06	−3 59	−6 08
Its mean	0 358	1 94	0 330	1 200	1 08	1 18
t	1 17	5 31	2 24	0 05	3 32	5 15
P		0 001	0 05		0 01	0 001

The plus sign in the difference of means indicates that the means in the present material are higher than those of Oberman and co workers

values The mean values of serum proteins and protein fractions in the patients who had and who had not received gamma globulin did not, in fact, differ Fortunately, the result of the study was such that it could not be interpreted as being caused by the administration of gamma globulin

draining ear with a cotton applicator Bacteria cultures were made over 70 times from ear secretions of 12 patients Cultures showed a monomicrobic infection in 60 cases a two to threefold bacterial mixed infection in ten ears In a few cases the culture did not grow The bacterial incidence was as follows staphylococcus aureus (the most common) st albus streptococcus pneumoniae haemophilus influenzae str beta haemolyticus str alpha haemolyticus corynebacterium pseudodiphtheriae pseudomonas pyocyanea st albus haemolyticus proteus mirabilis Escherichia coli Klebsiella and candida

The bacterial sensitivity was tested against 18 of the most frequently used antibiotics in addition to sulphathiazol and boric acid The classification was from a low of one to a high of five Mainly high scores were obtained with a plurality of drugs and an attempt was made to apply this information *Autovaccine therapy* was also tried in five children

The child usually benefited from these drugs and the relapse presented new bacteria On the other hand despite high sensitivity readings occasionally no improvement was achieved even by changing the wide spectrum antibiotics

Serum Protein Studies

The total serum proteins were determined by the Biuret method This and the paper electrophoresis were done at the State Serum Institute The electrophoresis apparatus was the Swedish LKB Corporation make The strips were dyed with bromthymol blue The values were measured with a Spinco Analysator The normal adult values were determined by this device in healthy donors to the Finnish Red Cross Blood Bank They are analogous to values published elsewhere There are no papers pertaining to normal values in Finnish children The ten year practical experience of the Helsinki University Children s Clinic (Wasz Hockert) and State Serum Institute (Saukkonen) as well as the material obtained in the ENT Clinic outside this series in various diseases seem to agree with the values of Oberman et al A comparison of our findings was therefore made with the latter material

At the time of the serum protein check ups the ears were draining and had discharged for at least two weeks Since all the cases had already been treated prior to the beginning of this study five of the cases were receiving gamma globulin The dosage employed in these 10 to 14 kg children had been modest generally being 2 ml of 15 per cent gamma globulin prepared by the Finnish Red Cross Blood Bank and given once every three or four weeks At the very most the child had received shots for five months When the child s weight and the time of medication (1 day 2 days a week and in two cases one month before samples were taken) are known we are able to theoretically calculate and also determine from the practical results of Finkel & Haworth that the giving of the drug hardly had influenced serum

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Review of the Electrophoresis Results

The total-protein amount has been higher in this series than in the control group (see Table 1). The statistical significance degree of this difference is indeed the lowest ($P < 0.05$) in infants one to two years old, but parallel observations concerning the age groups of under one-year-old and over three-year-old children support this finding. The relative share of albumin is noticeably greater in the present series. The result is highly significant in the one- to two-year-old infants, and a nearly similar difference is also presented by the other age groups. The relative decrease of globulin depends on the beta and gamma components, the decrease of which is statistically of high significance. This observation is analogous to that in the age groups of under one year and over three years.

DISCUSSION

The observed alteration in serum-protein pattern is of such a character that it is difficult to classify it other than as belonging to hypogammaglobulinemia. One cannot escape the thought that, besides the well-known but extraordinarily rare condition of agammaglobulinemia, it may exist in a milder form resembling defensive deficiency, and that this milder form, hypogammaglobulinemia, is considerably more common than true agammaglobulinemia. In recent years much has been written about the antibody deficiency syndrome, ADS, Antikorpermangelsyndrome, AMS (Escher & Barandum, 1960). Barandum *et al.* (1959) were able to collect 232 published cases, to which they added 31 cases of their own. Apparently the subject merits more attention by otologists.

It is indicated that this work should be continued with immunoelectrophoretic investigations.

This series is too small and the control time too short to justify any appraisal of the effect of gamma globulin therapy. Observations of individual cases, however, holds out promise of good results, provided that the administration of the drug is adequate.

ZUSAMMENFASSUNG

Die Ursachen und die Behandlung der rezidivierenden Mittelohrentzündungen in Kleinkindern sind mit besonderer Berücksichtigung auf den Zusammenhang zwischen Gammaglobulin und den infektiösen Krankheiten durchgegangen. Das vorliegende Material umfasst 18 konsekutive Fälle. Hypogammaglobulinämie scheint ein dominierender Faktor zu sein. Die Verabreichung von Gammaglobulin deutet auf bessere Heilungsresultate.

AUDIOLOGIC FINDINGS IN MENIERE'S SYNDROME

F HARBERT and I M YOUNG
Philadelphia Pa U S A

*From the Department of Otolaryngology (Head Prof F Harbert, M D)
Jefferson Medical College, Philadelphia*

Audiologic findings on the normal and affected side of thirty cases of unilateral Menière's syndrome are described All patients show continuous recruitment or above threshold and continuous recruitment There is no significant difference of aural overload threshold above audiometric zero between affected and opposite ears Abnormal tone decay and wide separation between pulsed and steady tone tracings indicating slow adaptation is not characteristic of hair cell lesions Shortly after an exacerbation of hearing loss Békésy audiograms may show slight separation and reduced amplitude of steady tone tracings in the area of increased hearing loss This is considered due to transient dendrite involvement causing rapid adaptation High tone hearing loss with slight separation and reduced amplitude of steady tone tracings is seen more often in long standing cases and attributed to secondary or unrelated dendrite involvement

The purpose of this study is to tabulate audiologic findings in typical unilateral Meniere's Syndrome If it can be shown that certain audiologic findings are always associated with Meniere's these findings may be presumed to be characteristic of a hair cell lesion Findings that are not constantly present might be assigned to secondary or unrelated nerve changes

Thirty cases of unilateral Ménière's disease aged 25 to 68 with duration of symptoms from 3 months to 16 years were studied Sixteen were male and fourteen female All gave a characteristic history of recurrent paroxysmal vertigo deafness and tinnitus Consecutive available cases from the files were taken after excluding those with a history of significant middle ear disease or acoustic trauma

PROCEDURE

Each subject was given standard pure tone air and bone audiometric tests Alternate loudness balance tests were performed to determine the presence of recruitment at three or more frequencies by a technique previously described (Harbert & Young 1962 *a*)

The laboratory equipment used for aural overload tests was a Maico aural overload tester The fundamental frequency used was 1000 cps The

This study was supported by N I H Grant B 2035

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Individual tracings showed a flat type curve in 24 cases gradual rise from low to high frequencies in three cases an abrupt drop at frequency 2000 cps in two cases and a gradual descent from low to high frequencies in one case. The last case showed a similar high tone loss in the opposite ear. Bone conduction loss approximated air conduction loss at all frequencies.

2 *Recruitment*

TABLE 2 *Type of recruitment*

Frequency	Above threshold and continuous recruitment	Continuous recruitment	Total recruitment (means) db
250	3	13	40
500	4	22	40
1000	6	23	40
2000	2	24	37
4000	3	16	39
8000	2	7	36

TABLE 3 *Degree of recruitment*

Frequency	Complete	Incomplete	Hyper
250	12	3	1
500	16	9	1
1000	16	13	—
2000	17	9	—
4000	11	8	—
8000	4	5	—

Each patient in this series showed recruitment by alternate loudness balance test at three or more frequencies. Tables 2 and 3 show number of tests at various frequencies. If total recruitment was 15 db or more 5 db above threshold a diagnosis of above threshold recruitment was made. Intensity above 5 db over threshold was increased by 15 db increments in the better ear and the affected ear balanced until the limit of the audiometer was reached. A diagnosis of continuous recruitment required the findings of approximately equal amounts of recruitment at two or more 15 db increments of comparison. No cases of above threshold recruitment without continuous recruitment were noted.

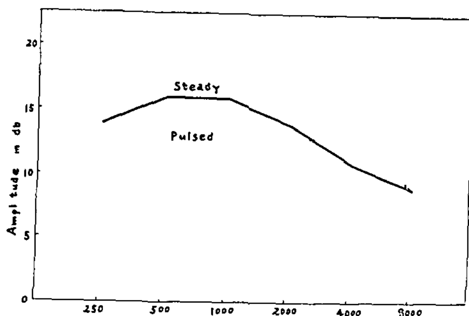


FIG. 1. Mean amplitude threshold tracings as a function of frequency (30 cases) unaffected ear.

exploring tone was set at 2004 cps. The technique used is the one recommended by Yantis (1956). The point of overload was recorded both as db above threshold and db above audiometric zero (ASA Standards).

In the tone decay test a continuous tone was presented at threshold for a period of 1 min. If the tone disappeared the examiner immediately increased the tone without interruption by 5 db. The difference in db at the end of a minute was recorded as the amount of decay. The time in seconds whenever the tone was increased was also recorded to indicate whether decay occurred early or late in the minute period (Harbert & Young *1962a*). Both continuously variable and fixed frequency Bekesy tracings were made for steady and interrupted tones on a Grason Stadler Model E 800-4 Audiometer at an attenuation rate of 5 db/sec. *During all tests the opposite normal* ear was masked with white noise at 100 db re 0.0002 dynes/cm² presented in a conventional earphone.

RESULTS

1. Air Conduction Loss

TABLE 1. *Thresholds of air conduction in db (means)*

Frequency	Affected ear	Opposite ear	Difference
250	45	3	[illegible]
500	46	2	44
1000	19	1	18
2000	44	6	38
4000	49	11	38
8000	48	14	34

Individual tracings showed a flat type curve in 24 cases gradual rise from low to high frequencies in three cases, an abrupt drop at frequency 2000 cps in two cases and a gradual descent from low to high frequencies in one case The last case showed a similar high tone loss in the opposite ear Bone conduction loss approximated air conduction loss at all frequencies

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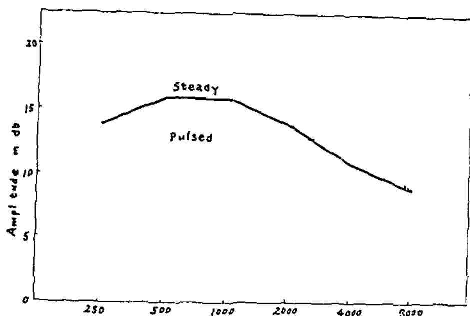


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8000	48	11	31

TABLE 5 *Comparison of Békésy tracing amplitudes*

Means of 30 cases Under Separation plus signs before Means indicate greater loss for steady tones Minus signs indicate greater loss for pulsed tones

	Amplitude steady		Amplitude pulsed		Separation	
Freq	Affected	Opposite	Affected	Opposite	Affected	Opposite
250	10±3 1	14±2 6	11±2 7	12±1 0	+3±0 9	+0 1±1 9
500	11±4 6	16±3 7	12±2 9	14±2 8	+4±1 8	−1 1±2 8
1000	11+2 5	16±3 3	12±3 0	14±2 8	+5±1 2	−0 4±2 9
2000	9±3 2	14±3 6	11±2 9	13±2 4	+5±2 0	−0 6±1 8
4000	9±2 0	11±4 0	12±2 4	13±4 0	+5±1 0	−0 1±2 7
8000	7±3 1	9±2 8	9±3 1	9±2 2	+5±1 1	+1 2±1 5

quencies below 3000 cps Fig 3 shows a better hearing for steady tones with a mean separation of 2 db between interrupted and continuous tones measured from bottoms of spikes (Harbert & Young 1962*b*)

Affected ear

Interrupted tones were heard better by about 5 db than steady tones (Table 5) Fig 2 shows that the mean amplitude of steady tone tracings is reduced at 2000 cps and above The amplitude of interrupted tones was consistently greater than that of continuous tones for all frequencies The 7 db mean steady tone amplitude of high frequencies compares with less than 5 db previously reported for an attenuation rate of 140 db per minute

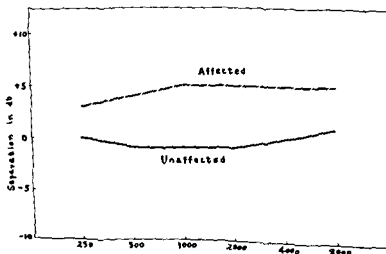


FIG 3 Mean separation between pulsed and steady tones Plus values pulsed tones show less loss then steady and Minus values pulsed tones show [illegible] steady

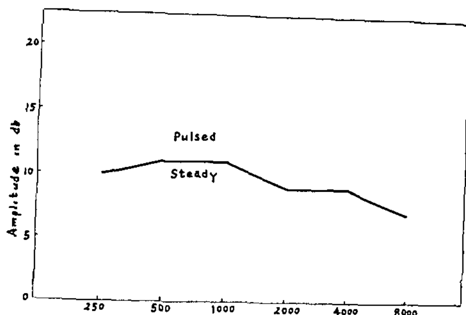


Fig 2 Mean amplitude as a function of frequency (30 cases) affected ear

3 Aural Overload

Table 4 *Aural overload at 1000 cps (means of 20 cases)*

Present data		Jantis (1956)	
	Range *Threshold to overload*		
Normal ear	61 7±6 2	Normals	52
Affected ear	18 8+9 0	Inner ear	21
	Overload Thresholds *Above audiometric zero*		
Normal ear	63 0±6 7	Normals	19
Affected ear	67 5+9 6	Inner ear	69

While it is true that inner ear lesions showing continuous recruitment have a restricted range absolute overload thresholds above audiometric zero in this series did not show a significant difference between affected and opposite unaffected ears

4 Bekesy Audiometry

Normal ear

The results of threshold recordings on the opposite normal or near normal side of all cases are presented in Table 5 and Fig 1 The mean amplitude of continuous tracings was 3 db higher than that of pulsed tracings for fre

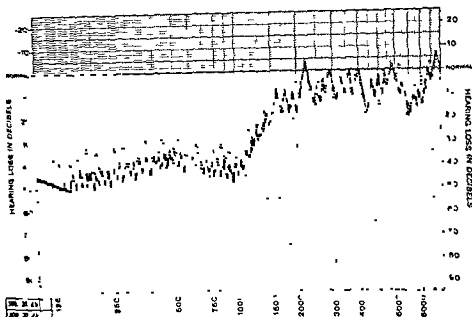


Fig 4 Reduced amplitude of steady tracings and slight separation of affected frequencies shortly after an exacerbation of hearing loss

rations are considered a manifestation of rapid adaptation due to involvement of dentrites (Harbert & Young, 1962*b*) Fig 4 shows reduced amplitude of steady tone tracings and slight separation at affected frequencies shortly after an exacerbation of hearing loss Fig 5 shows improved hearing with superposition of normal amplitude tracings two weeks later Hearing returned to normal in several weeks and remained normal until the next episode of hearing loss 5 months later when tracings were again similar to Fig 4 Hearing again returned to normal for a period of 13 months before repetition of the cycle At all times when hearing loss was present he showed pure complete continuous recruitment by the alternate loudness balance test A significant number of other cases in this series also showed superposition of normal amplitude tracings at some period

Perhaps there has been insufficient stress on the difference between continuous (linear) and above threshold (asymptotic) recruitment The former is associated with pure hair cell lesions with symptoms such as diplacusis, hyperacusis and distortion These symptoms are not a feature of above threshold recruitment

When an ear is exposed to loud sounds at non-damaging intensities, there is a temporary threshold shift During the threshold shift in normal ears the amplitude of steady tone tracings at the same frequency and above is reduced more than for pulsed tones and there is also slight separation between pulsed and steady tone tracings Ears with sensori-neural lesions already

(Lundborg 1952, Reger & Kos 1952). We have found that doubling the attenuation rate increases the amplitude in the ratio of 1 to 1.5 (Harbert & Young 1962*b*). Applying this ratio to this series, 7 db for 5 db per second would become about 4.6 db for 140 db *per minute*. Mean amplitudes of all frequencies on the affected side were always shorter than on the normal side whether continuous or interrupted tones were used (Table 5). It is interesting to note that mean *differences in* amplitude of interrupted tracings between affected and unaffected ears is about 2 db to 2000 cps and that there is no significant change at 4000 and 8000 cps (Table 5). Differences between steady *tracings* are of the order of 5 db in low and middle frequencies and only 2 db for 4000 and 8000 cps. This suggests that major differences are noted only in the steady tone tracings and these are less for frequencies above 2000 cps. High tone hearing loss, when present, tends to be symmetrical and is probably not related to unilateral Menière's.

The mean separation between bottoms of interrupted and steady tone continuously variable tracings varies from 3 db at low frequencies to 5 db at high (Fig. 3) and agrees with other reports (Jerger 1958, 1960*a*, *b*). Fixed frequency tracings at various frequencies showed no threshold drift.

5. *Tone Decay Test*

TABLE 6. *One minute tone decay in db* (*means*)

Frequency	Affected	Opposite
250	5	3
500	7	5
1000	9	4
2000	9	6
4000	8	8
8000	10	9

From Table 6 it is apparent that tone decay is not significant in Menière's. This is not in accord with some previous reports (Carhart 1957, Hood 1955) but agrees with the findings of Yantis (1959). With untrained observers tone decay of 5 or 10 db is often seen in normal and conductively deafened ears and is considered within normal limits in clinical practice.

DISCUSSION

After an exacerbation of reversible hearing loss, Békésy audiograms may show slight separation and reduced amplitude of steady tone tracings in the area of increased hearing loss. When hearing improves there is again superposition of normal amplitude tracings. Reduced amplitude and slight sepa-

2 All patients had continuous or above threshold and continuous recruitment at three or more frequencies

3 Aural overload threshold above audiometric zero of affected and opposite ears did not show significant differences

4 Unaffected ears showed slightly better hearing levels (2 db) for steady tone Békésy tracings than pulsed at attenuation rates of 5 db/sec Affected ears heard pulsed tones better by 5 db While means of this series showed reduced amplitude of steady tone tracings for frequencies above 1000 cps in the affected ears the opposite unaffected ears showed similar findings Low and middle frequency amplitude of steady tone tracings were reduced by 5 db and pulsed tones by 2 db in the involved ear Differences between ears in higher frequencies were less

5 Continuous recruitment as measured by the alternate loudness balance test is considered characteristic of Ménière's and a hair cell lesion When above threshold recruitment is also found it is considered an indication of additional involvement of peripheral dendrites

6 Early unilateral Ménière's cases when only hair cells are involved show superposition of normal amplitude pulsed and steady tone Békésy tracings Shortly after exacerbation of hearing loss there is reduced amplitude of steady tone tracings and slight separation This is considered due to transient dendrite involvement causing increase in rapid adaptation

7 Long standing unilateral Ménière's often show permanent high tone hearing loss which is usually symmetrical and perhaps unrelated Permanent reduction in amplitude of steady tone Békésy tracings and slight separation are considered manifestations of permanent dendrite injury causing abnormal rapid adaptation

ZUSAMMENFASSUNG

Audiologische Feststellungen von der *normalen und befallenden* Seite von *dreissig* Fällen einseitiger Ménièreschen Krankheitssyndroms sind *dargestellt* Alle Patienten zeigen ununterbrochenes Recruitment oder über der Horschwelle und ununterbrochenes Recruitment Da besteht kein bedeutsamer Unterschied der auralen Overload Schwelle wenn hoher als der audiometrische Nullpunkt zwischen dem *befallenden und gegenuberliegenden* Ohren Abnormale Verwesung des Tones (Tone Decay) und weite Separation zwischen den Zeichen von pulsierten und stetigen Tonen die langsame Adaptation anzeigen sind nicht charakteristisch der Haarzell Schadigung Kurz nach einer Verschlimmerung der Horverluste kann das Békésy Audiogram *eine geringere* Separation und verminderte Ausschlage der stetigen Zeichen in dem Gebiete des ver[illegible]

trachtet als eine vorubergehende d[illegible]

verursacht Horverlust in den hohe[illegible]

minderten Ausschlagen der stetigen [illegible] ist mehrmals in lang bestehenden Fallen gesehen und ist dem sekundarischen oder nicht verwandten Dendrit Verwicklung zuzuschreiben

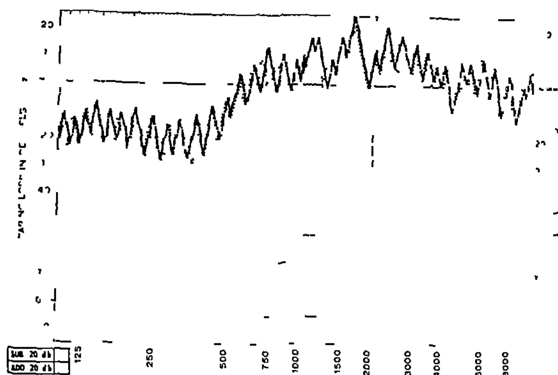


Fig 5 Superposition of normal amplitude tracings two weeks later

showing reduced amplitude of steady tone tracings and wide separation show a further reduction in amplitude of steady tone tracings. Recovery is rapid for pulsed tones and slower than normal for steady. This reduction in amplitude of tracings is considered a manifestation of increased rapid adaptation. Alternate loudness balance tests performed at this time characteristically show above threshold recruitment at the stimulated frequency. This is considered an example of a temporary receptive field lesion primarily affecting peripheral dendrites. Persistent continuous recruitment following acoustic trauma is considered due to hair cell injury. In Meniere's continuous recruitment is found in all cases and is attributed to a hair cell lesion. When there is also above threshold recruitment involvement of adjacent peripheral dendrites is postulated. Wide separation between pulsed and steady tone tracings and abnormal tone decay are considered manifestations of abnormal slow adaptation due to involvement of the rest of the neurone except for the telodendria. Peripheral dendrites and telodendria do not respond to the all or none principle (Bodian 1962, Eyzaguirre & Kuffler 1955) and can thus manifest rapid adaptation.

SUMMARY

1 The results of identical tests on the normal and affected side of thirty cases of unilateral Meniere's syndrome are described.

2 All patients had continuous or above threshold and continuous recruitment at three or more frequencies

3 Aural overload threshold above audiometric zero of affected and opposite ears did not show significant differences

4 Unaffected ears showed slightly better hearing levels (2 db) for steady tone Bekesy tracings than pulsed at attenuation rates of 5 db/sec Affected ears heard pulsed tones better by 5 db While means of this series showed reduced amplitude of steady tone tracings for frequencies above 1000 cps in the affected ears, the opposite unaffected ears showed similar findings Low and middle frequency amplitude of steady tone tracings were reduced by 5 db and pulsed tones by 2 db in the involved ear Differences between ears in higher frequencies were less

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Jefferson Medical College
Philadelphia 7, Penn, U S A

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UNILATERAL PARALYSIS OF THE SUPERIOR LARYNGEAL NERVE

K. FAABORG ANDERSEN and AA. MUNK JENSEN
Nykøbing F, Denmark

*From the Ear, Nose and Throat Department (Head: K. Faaborg Andersen, M.D.)
The Central Hospital, Nykøbing F.*

It is shown by electromyographic investigations that isolated paralysis of superior laryngeal nerve does not result in a slack vocal cord with wavy edges, as was previously accepted, but in an oblique glottis, the posterior end of which points toward the paretic side, while the posterior part of the paretic vocal cord is in a lower position than its opposite.

It has long been evident that the cricothyroid muscle is innervated only through the external branch of the superior laryngeal nerve (Schech 1873, Exner 1884, Katzenstein 1892, Wagner 1892, Grabower 1898) and most observations indicate that this is the only muscle which is innervated through the superior laryngeal nerve (Lemere 1933, Murtagh 1945, Negus 1947, King & Gregg 1948, Armstrong & Hinton 1951).

The isolated paralysis of the superior laryngeal nerve has previously been considered a rarity, for which reason it is not often referred to in earlier literature. When mentioned, the laryngoscopic picture is described as follows: On the paretic side the vocal cord appears slack with wavy, irregular edges, especially during phonation (Mygind 1906, Luchsinger 1942).

In most textbooks the complaint is similarly described (Jackson 1946, Ballinger 1947, Blegvad 1949, Scott Brown 1952, Luscher 1956).

A laryngoscopic picture such as this is very unusual and unilateral isolated paralysis of the superior laryngeal nerve was consequently considered a rarity. This is remarkable, as the combined paralysis of the superior and the inferior laryngeal nerve is not uncommon. In strumectomy one often gets dangerously close to the superior laryngeal nerve, and therefore isolated paralysis of this nerve might occur.

The explanation of this incongruity is undoubtedly that isolated unilateral paralysis of the superior laryngeal nerve is not indicated by a slack vocal cord with wavy, irregular edges, but by an oblique glottis ...

Fig. 1.

The vocal process of the arytenoid cartilage will furthermore during phonation lie in a somewhat lower position on the paretic than on the normal side, as is outlined in Fig. 2.

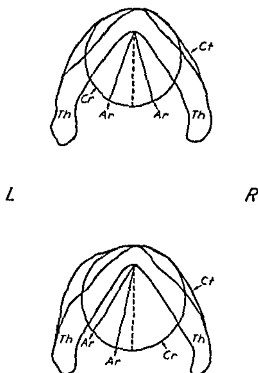


FIG 1 Sketch of unilateral function of oblique part of the cricothyroid muscle Horizontal cross section *Th*, thyroid cartilage *Cr*, cricoid cartilage *Ct*, right cricothyroid muscle *Ar*, arytenoid cartilage The upper sketch shows a normal larynx at rest In the lower sketch is shown the effect of stimulation of the right, or paralysis of the left cricothyroid muscle on the position of glottis Note that the posterior part of glottis points toward the left

Whether an oblique glottis is always due to isolated paralysis of the superior laryngeal nerve, or whether a congenital form of "oblique glottis" exists is another question There are indications that such a congenital form does exist, the picture of this differing in certain aspects from that of paralysis of the superior laryngeal nerve

Having come to the conclusion that unilateral paralysis of the superior laryngeal nerve gives a picture as outlined above we have discovered, that this paralysis is not so unusual as previously assumed During the last 12 months we, in this department, have seen a total of five cases of this complaint

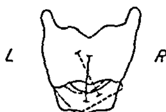


FIG 2 Sketch of unilateral function of vertical part of the cricothyroid muscle Frontal cross section Stimulation of the right or paralysis of the left cricothyroid muscle The cricoid cartilage being raised on the right but not on the left side the right arytenoid will be in a higher position than the left one

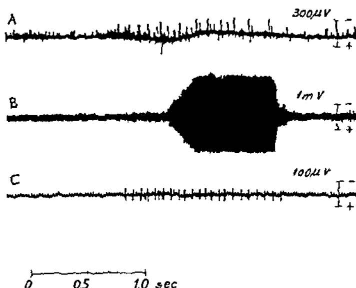


Fig 3 Electrical activity in the cricothyroid muscles during phonation with simultaneous microphone recording *A*, The action potential pattern in the (normal) left cricothyroid muscle *B*, Microphone recording C, The action potential pattern in the (paretic) right cricothyroid muscle Patient No 4, a 78 year old man with pronounced obliquity of glottis, the posterior part of which pointed toward the right

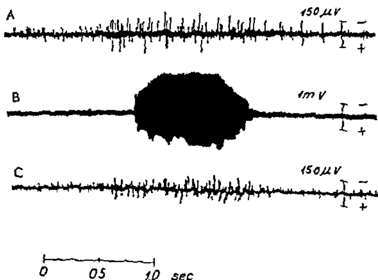


Fig 4 Electrical activity in the *cricothyroid* muscles during phonation with simultaneous microphone recording *A*, The action potential pattern *in the left* cricothyroid muscle *B*, Microphone recording C, The action potential pattern in the right *cricothyroid* muscle Same patient as in Fig 3 one month later, glottis having regained its normal straight shape

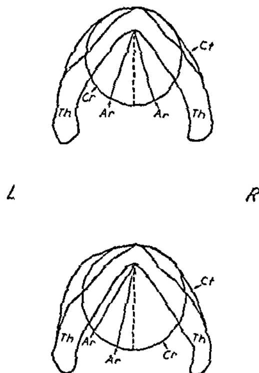


Fig 1 Sketch of unilateral function of oblique part of the cricothyroid muscle Horizontal cross section *Th*, thyroid cartilage *Cr*, cricoid cartilage *Ct*, right cricothyroid muscle *Ar*, arytenoid cartilage The upper sketch shows a normal larynx at rest In the lower sketch is shown the effect of stimulation of the right, or paralysis of the left cricothyroid muscle on the position of glottis Note that the *posterior part of glottis points toward the left*

Whether an oblique glottis is always due to isolated paralysis of the superior laryngeal nerve, or whether a congenital form of "oblique glottis" exists is another question There are indications that such a congenital form does exist, the picture of this differing in certain aspects from that of paralysis of the superior laryngeal nerve

Having come to the conclusion that unilateral paralysis of the superior laryngeal nerve gives a picture as *outlined above we have discovered*, that this paralysis is not so unusual as previously assumed During the last 12 months we in this department, have seen a total of five cases of this complaint

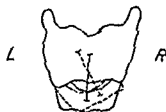


Fig 2 Sketch of unilateral function of vertical part of the cricothyroid muscle Frontal cross section Stimulation of the right or paralysis of the left cricothyroid muscle The cricoid cartilage being raised on the right but not on the left side the right arytenoid will be in a higher position than the left one

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E N T Department, The Central Hospital, Nykøbing F, Denmark

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One of these was caused by strumectomy, one by cancer of the thyroid gland, one by superior glandular metastasis of the neck and the last two probably by neuritis In all five cases the patients had a relatively good though somewhat deep and monotonous speaking voice, while the singing voice was poor in four cases Intrinsic laryngeal anaesthesis was found in four cases, while this could not be proved in the fifth case

The diagnosis was based not only on the characteristic oblique glottis but also on electromyography

One of these cases deserves particular mention, that of a 78 year old man who contracted a right sided paralysis of the superior laryngeal nerve supposedly due to neuritis It was remarkable that in this case the paresis receded and that the case could be followed after cessation of the paresis

The electromyogram (Fig 3) was recorded during the right sided paralysis of the superior laryngeal nerve Laryngoscopy showed at the time a pronounced obliquity of glottis, the posterior part of which pointed towards the right The right arytenoid cartilage was lower than the left The electric activity of the two cricothyroid muscles was examined by insertions of needle electrodes in various places of the muscles at different times, and these examinations showed similar results every time (see Fig 3)

The electromyogram (Fig 4) was recorded one month after the first electromyogram At that time the paresis had receded, the glottis having regained its normal straight shape, and there being no difference in the height of the two arytenoids

ZUSAMMENFASSUNG

Durch elektromyographische Untersuchungen wird gezeigt, dass isolierte, einseitige Lahmung des Nervus laryngeus superior nicht ein entspanntes Stimmband mit wellenformigen Randern ergibt wie fruher beschrieben, sondern eine schiefe Stimmritze mit dem *Aryknorpel ruckwarts nach der gelahmten Seite verschoben und tiefer* stehend als die gegenseitige

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E N T Department, The Central Hospital,
Nykøbing F, Denmark

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ON THE TREATMENT OF CHRONIC POSTOPERATIVE OTORRHEA

A. J. BURGEMEESTRE
Breda, Netherlands

From the E.N.T. Departments (Heads: A. J. Burgemeestre and J. van Dam) of the Deaconess Hospital (Dir.: Dr. H. Buys) and the St. Laurens Hospital (Dir.: A. M. Bakers), Breda

A description of a surgical technique for the treatment of chronic postoperative otorrhea is given. The operation consists of meticulous removal of all pathological contents from the operative cavity, followed by closure of the auditory canal by *suturing its membranous walls together*. Eleven ears were operated upon. All ears became dry.

In an article on the prevention of chronic postoperative otorrhea (Burgemeestre 1963) I stressed the importance of adequate preoperative treatment and worked out a new tympanoplastic technique. The essential feature of this technique is the preservation of the posterior wall of the bony auditory canal. With this technique excellent results in the prevention of chronic *postoperative otorrhea were obtained*.

But what treatment should be given in cases in which the posterior wall of the bony auditory canal has already been removed in a previous operation and in which *postoperative otorrhea has developed?*

The most "radical" solution consists of meticulous removal of all pathological contents from the operative cavity, followed by closure of the auditory canal by means of suturing its membranous walls together. This method is related to the procedure described by Rambo (1958).

TECHNIQUE

After an incision according to Heermann (Zollner & Altmann 1960) the auricle is clapped downwards. The operative cavity can now thoroughly be inspected. All squamous epithelium (epithelial *ingrowths from the auditory* canal, skin grafts, remnants of the drum membrane, cholesteatoma matrix) has to be removed carefully. Likewise all diseased bone, granulations, *polyps* and remnants of the ossicles have to be taken away. The mucous membrane of the tympanic cavity and of the distal (tympanic) part of the Eustachian tube is removed with a curette. The skin lining the osseous part of the auditory canal is completely excised. The remaining outer portion of the auditory canal is closed by suturing the posterior and anterior skin edges

together The operative cavity is dusted with an antibiotic powder Finally, the auricle is moved back to its normal position and the remaining wound is closed with sutures A polyethylene tube is left in place in the retro auricular part of the wound for a few days as a temporary drain The sutures are removed after 10 days

RESULTS

In 1962 the operation was performed on 11 ears In each case there was a long standing monaural postoperative otorrhea with no useable hearing on the affected side the hearing on the other side being normal In one case the discharging ear had been operated upon elsewhere 12 times without success All ears operated upon by the method described above became dry in about two weeks After the removal of the sutures there was in two cases a small dehiscence of the wound edges in the auditory canal Fortunately the dehiscence closed spontaneously in both cases

After the operation all patients remained under observation for a period varying from 6 months to 1 year During this admittedly rather short period no recurrences were seen and there was no need for after treatment

COMMENT

In radical mastoidectomies tympanoplasties and fenestration operations postoperative otorrhea is often the result of disturbed epidermization of the mastoid cavity In many cases the operation may have cured the otitis media but unfortunately has produced at the same time a badly epidermized operative cavity

Now the new operative technique aims to cure the postoperative otorrhea by means of the removal of all epidermis from the cavity and the closure of the auditory canal The removal of epidermis must be performed with great care Otherwise there is a risk of postoperative cholesteatoma, which would manifest itself by redness and bulging of the tissues overlying the cavity (auricle retro auricular skin) and which would require another operation

At the same time one should carefully remove all otitis media pathology as well as the mucosa of the tympanic cavity and the distal (tympanic) part of the Eustachian tube Granulation tissue is now assumed to fill the closed cavity and the tympanic portion of the Eustachian tube is expected to obliterate

It will be evident that no useable hearing can be expected in an ear that has been submitted to the operation described above On the other hand one can expect to bring the otorrhea to an end in most cases It must of course be made clear to the patient what he can and what he cannot hope from the operation In my opinion it is justified to recommend the operation when the following requirements are fulfilled

1. there is a long standing postoperative otorrhea, resistant to other therapy,
2. there is a considerable deafness on the affected side,
3. the hearing in the other ear is normal

ZUSAMMENFASSUNG

Es wird eine Beschreibung einer chirurgischen Technik zur Behandlung von postoperativer Otorrhoe gegeben. Die Operation besteht aus einer gründlichen Ausräumung der Operationshohle und Verschliessung des äusseren Gehorganges. 11 Ohre wurden mit gutem Erfolg operiert

RÉSUMÉ

Une technique chirurgicale pour le traitement de l'otorrhée postopératoire est décrite. L'opération consiste d'un nettoyage précis de la cavité opératoire et de la fermeture du conduit auditif. Onze oreilles furent opérées avec de bons résultats dans tous les cas

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STUDIES ON HABITUATION OF VESTIBULAR REFLEXES

VII Habituation in light of calorically induced nystagmus, laterotorsion, and vertigo in man

B Forssman
Lund, Sweden

From the Department of Neurology (Acting Head Doc O Berg) and the Department of Otolaryngology (Head Prof Hj Koch), University of Lund

Fifteen normal subjects received 12 consecutive caloric irrigations with water of 30 C in the right ear The calorizations were performed in full light except the 1st and the 12th ones used as tests to make possible comparisons with a previously reported series with all irrigations made in darkness Four qualities were compared (1) eye velocity, (2) duration of nystagmus (3) laterotorsion and (4) vertigo

The tests revealed the same extent of response decline from calorizations in light as in darkness and also the same order of habituation rate

When the light was turned on there was a sudden decrease and when it was turned off a sudden increase of nystagmus and laterotorsion but not of vertigo which declined in the same manner independently of light and darkness At the end of the habituation trials in light, laterotorsion was often the only observable effect of the calorizations

With increasing habituation the dysrhythmia of nystagmus increased more in light than in darkness

INTRODUCTION

Normal subjects exposed in darkness to repeated monoaural isothermal calorizations presented a successive decrease at different rates of maximum eye velocity duration of nystagmus maximum laterotorsion and maximum vertigo They also showed an increase of the dysrhythmia of nystagmus as the habituation proceeded This was shown in a previous study on habituation in darkness (Forssman Henriksson & Dolowitz 1963)

The material constituting the dark series has now been supplemented by the light series in which all irrigations were performed in full light, except the first and the last ones These were conducted in darkness for comparison with the dark series

The aims of the present study of habituation in light are (1) to determine the effect of light on the habituation of eye velocity duration of nystagmus laterotorsion and vertigo and (2) to compare the dysrhythmia of nystagmus in light with that in darkness

This investig[illegible]s supported by the Medical Faculty University of Lund

In the present paper references will often be made to results from the dark series in the above mentioned previous paper (Forssman, Henriksson & Dolowitz 1963).

HISTORY

A survey of the literature on the habituation of nystagmus by successive calorizations and on the response decline (RD) of vertigo and vestibulo-spinal reaction to repeated vestibular stimuli has been given by Forssman, Henriksson & Dolowitz (1963).

For the present study it remains to consider the literature on a comparison between the nystagmus habituation in light and in darkness.

There has been no satisfactory answer to the question of whether the habituation increases or decreases when influence of light is added to repeated vestibular stimuli. In published analyses important factors have often been neglected, such as:

1. Visual impulses might influence the habituation irrespective of optokinetic mechanisms.

2. Visual impressions give rise to optokinetic impulses unless the surroundings are devoid of contours. These impulses might influence the habituation in different ways depending on the experimental conditions.

When a subject is rotated but not the surroundings, the optokinetic impulses increase per-rotatorily and decrease post-rotatory nystagmus. If the test subject is rotated together with the surroundings, both the per- and the post-rotatory nystagmus are decreased (Loeb 1907). On calorization the optokinetic impulses inhibit the induced nystagmus.

3. When, for evaluation of the habituating effect, two series of test subjects are compared, the one habituated in darkness and the other in light, the tests before and after acquisition should be performed in darkness in both series according to the following considerations.

It has not been proved whether light or optokinetic impulses or both contribute to the habituation due to repeated vestibular stimuli. If the mechanisms of light have such an action, there will also be retention of the effect. The test in darkness after acquisition in light will then show a greater RD than after acquisition in darkness. If the effect of light, however, is only accidental and not habituating, it follows that the test in darkness after acquisition in light will show about the same RD as after acquisition in darkness.

Abels (1906), Griffith (1920), Maxwell & Pilz (1924), King (1926) and Mowrer (1934*b*) have compared the habituation of nystagmus in light with that in darkness in rotation experiments.

Abels, King & Mowrer used pigeons, which showed a head nystagmus changing the vestibular stimulation due to rotation. In some of their series King & Mowrer eliminated this source of error by performing the acquisition with the heads of the pigeons kept in a fixed position.

None of these authors performed the comparative tests on habituation in

light and darkness under identical conditions except Mowrer, who conducted them in dim light but not in complete darkness

Because of the above mentioned inaccuracies it is difficult to draw valid conclusions from the reported comparisons between habituation in light and in darkness The results of these authors only indicate that nystagmus is more affected when influences of light including optokinetic mechanisms are added to rotatory stimuli but not if the degree of habituation is thereby changed

Proctor & Fernández have recently (1963) made a study of the habituation of nystagmus by repeated caloric irrigations in blindfolded cats They found that the general pattern of the RD was similar to that described by Henriksson, Kohut & Fernandez (1961) in cats habituated in light Their conclusion was that the vision may have some influence in developing habituation but that it is not a crucial factor

METHODS AND MATERIAL

The methods were the same as those described by Forssman Henriksson & Dolowitz (1963) except that most of the calorizations were performed in light (see below)

To the dysrhythmia grades from 0 to 3 has now been added

Grade 4 – No discernible signs of nystagmus

The material consisted of fifteen normal volunteers other than those *in* the dark series eight men and seven women aged 16–56 years

Each subject had one trial for acquisition of habituation, consisting of 12 consecutive irrigations of the right ear with water of 30°C for 40 *seconds* at five minute intervals Only the first and the twelfth calorization were made in darkness all the ten intervening ones in full light *(the light series)*

Four qualities were compared (1) Maximum eye velocity (2) duration of nystagmus (3) maximum laterotorsion and (4) maximum vertigo The dysrhythmia of nystagmus was treated separately

RESULTS

It should be pointed out that the values for vertigo and dysrhythmia are only approximate owing to the limited and not equidistant evaluation scales (Lidvall 1961 *b*) The reliability of the conclusions regarding these two qualities is therefore somewhat restricted

The values for maximum eye velocity duration of nystagmus, maximum laterotorsion and maximum vertigo of all irrigations are given in the appendix Tables 1–4

The means of the values for every order of irrigation and for each of the four qualities are graphically represented in Fig 1

If Fig 1 is compared with the corresponding Fig 1 for the dark series it will be seen that maximum eye velocity, duration of nystagmus, and

In the present paper references will often be made to results from the dark series in the above mentioned previous paper (*Forssman, Henriksson & Dolowitz 1963*).

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A survey of the literature on the habituation of nystagmus by successive calorizations and on the response decline (RD) of vertigo and vestibulo spinal reaction to repeated vestibular stimuli has been given by Forssman, Henriksson & Dolowitz (1963).

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There has been no satisfactory answer to the question of whether the habituation increases or decreases when influence of light is added to repeated vestibular stimuli. In published analyses important factors have often been neglected, such as:

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It has not been proved whether light or optokinetic impulses or both contribute to the habituation due to repeated vestibular stimuli. If the mechanisms of light have such an action, there will also be retention of the effect. The test in darkness after acquisition in light will then show a greater RD than after acquisition in darkness. If the effect of light, however, is only accidental and not habituating, it follows that the test in darkness after acquisition in light will show about the same RD as after acquisition in darkness.

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Abels, King & Mowrer used pigeons which showed a head nystagmus changing the vestibular stimulation due to rotation. In some of their series King & Mowrer eliminated this source of error by performing the acquisition with the heads of the pigeons kept in a fixed position.

None of these authors performed the comparative tests on habituation in

TABLE 1 *RD from the 1st to the 12th irrigation*

M = mean value of the 12th irrigation in per cent of the 1st. The lower the *P* value the higher the significance of an RD

	M	P value
Maximum eye velocity	44.1	$P < 0.001$***
Duration of nystagmus	73.8	$P < 0.001$***
Maximum laterotorsion	60.5	$0.01 < P < 0.05$*
Maximum vertigo	16.1	$P < 0.001$***

The response declines are thus about the same as in the dark series. The only difference is that the RD of maximum laterotorsion seems to be more reliable in the dark series (significant*** as against significant*). This difference might, however, be due to chance since laterotorsion is the most variable of the four reactions.

(b) *The order in rate of RD*

A comparison of the four qualities has been made with regard to the steepness of the relative declines from the 1st to the 12th irrigation. The Wilcoxon matched pairs signed ranks test has been applied in this study. (As to vertigo, three subjects with no dizziness at all from irrigation no. 1 were omitted because there was no possibility of any further decrease.)

The analysis showed that the RD of

max. vertigo is greater than that of max. eye-velocity	($0.001 < P < 0.01$**)
max. vertigo is greater than that of duration of nystagmus	($0.001 < P < 0.01$**)
max. vertigo is greater than that of max. laterotorsion	($0.001 < P < 0.01$**)
max. eye velocity is greater than that of duration of nystagmus	($P < 0.001$***)
max. eye velocity is greater than that of max. laterotorsion	($0.01 < P < 0.05$*)
max. laterotorsion is greater than that of duration of nystagmus	($P > 0.05$ not sign.)

Conclusions. The order of the habituation rate from the greatest to the slightest is (1) vertigo, (2) eye velocity, (3) duration of nystagmus equal to laterotorsion.

As in the dark series, duration of nystagmus and of laterotorsion show about the same degree of RD.

II. Changes of RD by Turning the Light On and Off

On two occasions there was a change of illumination in the lightseries, viz. after the 1st irrigation, when light was turned on, and after the 11th ir-

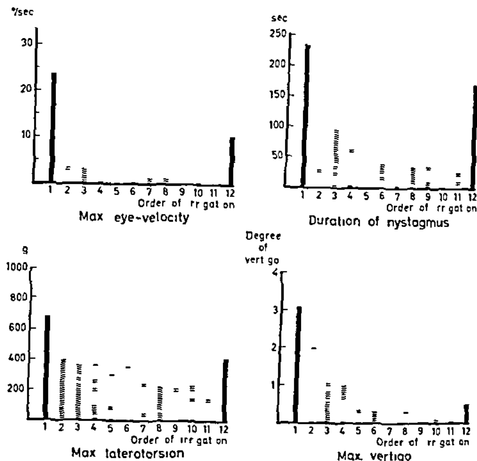


Fig. 1. Diagrammatic representation of maximum eye velocity, duration of nystagmus, maximum laterotorsion and maximum vertigo following repeated calorizations. Mean values from fifteen normals, all irrigated 12 consecutive times for 40 seconds with water of 30° C in the right ear. The first and the last irrigations made in darkness, all the others in light.

maximum laterotorsion are more depressed during the calorizations in light than in darkness (irrigations 2–11). This is particularly noticeable in the case of the maximum eye velocity. With the last calorization in darkness the reactions rise again but do not reach their initial levels.

I. Determination of the Habituation of the Different Qualities

This determination was performed by comparing the relative decrease from the 1st to the 12th irrigation.

(a) The establishment of an RD

The significance of this decline has been calculated according to the sign test. See Table 1.

Conclusion. There is an RD of all four qualities.

As seen from Tables 1–4 of the appendix the last value for maximum eye velocity and duration of nystagmus is always less than the first, for maximum vertigo never greater than the first, and for maximum laterotorsion sometimes as great as or even greater than the first.

IV Comparison of the Habituation between the Light and the Dark Series

As has been shown the pronounced decrease of nystagmus is particular, but also of laterotorsion during calorization in light (irrigations 2–11), shows a rebound phenomenon when the light is turned off (12th irrigation) The following question then arises Is this rebound complete? In other words Would the end result be the same if all calorizations had been performed in darkness?

In an attempt to solve this problem a comparison was made between the light and dark series of the relative declines from the 1st to the 12th irrigations

According to the Mann Whitney U test the P values are above 0 05 for all the four qualities It is thus evident that there is no significant difference of RD between the light and the dark series

Conclusion Light does not influence the degree of RD as judged from the final outcome in darkness This is valid for all four qualities

V *The Dysrhythmia of Nystagmus*

Forssman Henriksson & Dolowitz found (1963) that there was a growing dysrhythmia of nystagmus with increasing habituation in darkness This dysrhythmia was moderate, not exceeding 2 grades Only when the calorizations are performed in light, dysrhythmias of grades 3 or 4 may appear

The grade of dysrhythmia in each calorization is given in appendix, Table 5

It seems doubtful if the failing of a nystagmus reaction should be considered the most extreme form of dysrhythmia (grade 4) or if it should be evaluated as a special phenomenon not closely connected with the dysrhythmias Calculations have been made with respect to both of these possibilities As the results however, point in the same direction whether using an evaluating scale of 0–4 or 0 3, and as they admit of the same conclusions, the first alternative is here accounted for

It is apparent from Table 5 in the appendix that the dysrhythmias increase during the course of the calorizations in light

To make easier a comparison of dysrhythmias in corresponding parts of the light and dark series the term of dysrhythmia quotient has been used for the sum of grades of dysrhythmia divided by the number of irrigations in the part of the series considered See Table 3

There are more dysrhythmias in the total light series than in the total dark series This difference is significant***

To find out if this difference is really due to the influence of light, each series has been divided into two parts one in which the corresponding irrigations in both series were made in darkness (only 1 and 12) and the other in which they were performed in darkness in the dark series and in light in the light series (from no 2–11 inclusive) See Table 3

TABLE 2. *The differences between the light and the dark series in the relative decreases from the 1st to the 2nd and in the relative increases from the 11th to the 12th irrigations according to Mann-Whitney's U test.*

The lower the P value, the higher the significance of such differences.

	Decrease from 1st to 2nd irrig.	*Increase from 11th to 12th irrig.*
Maximum eye velocity	$P<0.001$***	$P<0.001$***
Duration of nystagmus	$P<0.001$***	$P<0.001$***
Maximum laterotorsion	$0.001<P<0.01$**	$0.001<P<0.01$**
Maximum vertigo	*$P>0.05$ not sign.*	*$P>0.05$ not sign.*

rigation when it was turned off. In the dark series there were no such changes.

The differences in the relative changes between the light and the dark series on these two occasions have been calculated according to Mann-Whitney's U test. See Table 2.

Conclusions. The change from darkness to light has an immediate inhibiting effect on maximum eye velocity, duration of nystagmus and maximum laterotorsion.

The change from light to darkness has an immediate increasing effect on the same qualities.

The vertigo does not show significant changes when the light is turned on or off.

III. RD during the Irrigations in Light 2–11

Calculations of RD in these conditions have a restricted value, firstly because the important changes between the 1st and the 2nd and between the 11th and the 12th irrigations are not taken into account. Secondly, it is not quite easy to measure exactly such feeble nystagmus reactions as often appear on calorization in light. The validity of conclusions on nystagmus in light is therefore somewhat restricted.

The following conclusions, however, are admissible.

(*a*) When the declines in light are compared with those in darkness, calculations according to the Mann-Whitney U test show that the decrease of nystagmus (velocity and duration) is relatively greater during these irrigations in light than in darkness (significant***).

(*b*) A comparison *between the different qualities of the steepness* of the RD shows, according to Wilcoxon's matched pairs signed ranks test, that nystagmus (velocity and duration) presents a greater rate of decrease than laterotorsion (significant*). As a matter of fact, nystagmus and usually also *vertigo were often found* to be absent, with laterotorsion still present during calorization in light.

IV *Comparison of the Habituation between the Light and the Dark Series*

As has been shown the pronounced decrease of nystagmus is particular but also of laterotorsion during calorization in light (irrigations 2 11) shows a rebound phenomenon when the light is turned off (12th irrigation) The following question then arises Is this rebound complete? In other words Would the end result be the same if all calorizations had been performed in darkness?

In an attempt to solve this problem a comparison was made between the light and dark series of the relative declines from the 1st to the 12th irrigations

According to the Mann Whitney U test the *P* values are above 0 05 for all the four qualities It is thus evident that there is no significant difference of BD between the light and the dark series

Conclusion Light does not influence the degree of BD as judged from the final outcome in darkness This is valid for all four qualities

V *The Dysrhythmia of Nystagmus*

Forssman Henriksson & Dolowitz found (1963) that there was a growing dysrhythmia of nystagmus with increasing habituation in darkness This dysrhythmia was moderate not exceeding 2 grades Only when the calorizations are performed in light dysrhythmias of grades 3 or 4 may appear

The grade of dysrhythmia in each calorization is given in appendix, Table 5

It seems doubtful if the failing of a nystagmus reaction should be considered the most extreme form of dysrhythmia (grade 4) or if it should be evaluated as a special phenomenon not closely connected with the dysrhythmias Calculations have been made with respect to both of these possibilities As the results however, point in the same direction whether using an evaluating scale of 0–4 or 0–3 and as they admit of the same conclusions the first alternative is here accounted for

It is apparent from Table 5 in the appendix that the dysrhythmias increase during the course of the calorizations in light

To make easier a comparison of dysrhythmias in corresponding parts of the light and dark series the term of dysrhythmia quotient has been used for the sum of grades of dysrhythmia divided by the number of irrigations in the part of the series considered See Table 3

There are more dysrhythmias in the total light series than in the total dark series This difference is significant***

To find out if this difference is really due to the influence of light each series has been divided into two parts one in which the corresponding irrigations in both series were made in darkness (only 1 and 12) and the other in which they were performed in darkness in the dark series and in light in the light series (from no 2 11 inclusive) See Table 3

TABLE 3 *Dysrhythmias in the light and the dark series*

Dysrhythmia quotient = sum of grades of dysrhythmias divided by the number of irrigations in the part of the series considered. The smaller the P value calculated according to the χ^2 test the higher the significance of differences with respect to dysrhythmia between the light and the dark series

Irrigations	Dysrhythmia quotient Light series	Dark series	P value
From no 1–12 incl	2 18	0 12	$P < 0.001$***
Only 1 and 12	0 13	0 37	$P > 0.05$ not sign
From no 2 11 incl	2 53	0 43	$P < 0.001$***

This analysis makes it evident that there is no difference in dysrhythmia between the two series when *irrigations in darkness are compared (only 1 and 12)* but highly significant ones when irrigations in light and darkness are *compared (from no 2–11 inclusive)* Thus the influence of light increases the dysrhythmias

Conclusions There is a growing dysrhythmia with increasing habituation The influence of light increases dysrhythmia More pronounced grades of this phenomenon appear only in light

DISCUSSION

In this study of habituation to repeated calorizations in light the first and the last irrigation were performed in darkness in order to make possible a *comparison of the results from the reported dark series (Forssman Henriksson & Dolowitz 1963)*

1 During the trials for habituation there is a sudden decrease of eye velocity duration of nystagmus and laterotorsion when light is turned on and a sudden increase of the same qualities when it is turned off When the habituating calorizations are only performed in darkness there are as a rule no such sudden changes in these reactions

The habituation of vertigo however seems to proceed in about the same manner independently of light and darkness

This also indicates that the habituation of vertigo is independent of whether the nystagmus reaction is intense as in darkness or feeble as in light The nystagmus would thus not be directly involved in the habituation of vertigo

2 At the end of calorization in light nystagmus and also vertigo often vanish completely *while laterotorsion usually shows moderate reactions* In irrigations no 10 for instance there is no obvious nystagmus in 10 out of 11 test *subjects but a clear cut laterotorsion Nine out of these 10* subjects did not feel any vertigo either A moderate laterotorsion was thus the only observable effect of the calorizations

3 The cause of the depressed nystagmus during calorization in light as compared to darkness and its sudden changes when light is turned on and off can at least partially be explained by the optokinetic mechanism During the induced vestibular nystagmus with say, the slow component to the right, the subject has the impression that his surroundings move to the left As the illuminated room is not devoid of contours there are conditions for inducing an optokinetic nystagmus with the slow phase to the left i e the vestibular nystagmus will be counteracted by optokinetic impulses

The laterotorsion is also subject to sudden changes when light is turned on and off It is probable that the depressed vestibulo spinal reactions in light directly result from the visual impulses and not indirectly from the decreased eye movements since it has earlier been shown (Henriksson Forssman & Dolowitz 1962) that there is no significant correlation between nystagmus and laterotorsion The visual impulses make possible a better orientation than in darkness and thereby also a correction of vestibulo spinal reactions resulting in decrease of laterotorsion

4 The greater depression of nystagmus and laterotorsion during calorization in light than in darkness ceases when the light is turned off

The RD and also the order of habituation rate of the four qualities are thus the same in light as in darkness as judged from the initial and the final tests in darkness

The habituation is thus independent of light whose influence on nystagmus and laterotorsion is only transitory and entirely reversible

It should be stressed that the habituation of eye velocity is greater than that of laterotorsion in light as well as in darkness

5 The dysrhythmia of nystagmus increases with repeated calorization This phenomenon is probably caused by a growing central inhibition now and then broken through by stimuli in the nature of arousal alertness or attention (cf Mowrer 1934*a* Wendt 1951 Tidvall 1961*a*, Collins *et al* 1962) It is probable that the augmentation of dysrhythmia in light as compared to darkness depends on the addition of inhibitory visual impulses, including optokinetic ones

6 Habituation phenomena within the vestibular system are not found only in the laboratories but also in daily life and might also be of importance for interpreting certain pathological findings

In some professions it is especially noticeable Tschiassny (1957) thus observed that ballet dancers after rotation in a chair during darkness showed weak nystagmus of short duration but a normal past pointing (i e vestibulo spinal) reaction The state of the dancers was thus the same as can be elicited in normals on repeated calorizations

A greater degree of habituation was found by McCabe (1960) who reported that well trained figure skaters showed no nystagmus and claimed to have no vertigo on rotatory and caloric examinations They could perform correct tape walking after rotation in a chair, even blindfolded

In Ménière's disease it is not unlikely that the habituation phenomenon is in part responsible for the usual decrease of the severity of the attacks

A similar pattern of habituation to that reported in this and the preceding paper (Forssman, Henriksson & Dolowitz, 1963) might conceivably arise from other sources than the labyrinth (e g. from the eyes), provided that the repeated stimuli influence the reflexes governing the equilibrium and that these are useless or inadequate. Such a theory is based on the evidence from experiments on cerebral lesions (Hernández-Peón & Brust-Carmona, 1961) This evidence indicates that the habituation requires the functional integrity of the brain stem reticular formation, which is open to modifying influences from different sources

Finally, the same pattern of caloric response as can be elicited from repeated vestibular stimulations is frequently found in persons suffering from blindness or congenital nystagmus The mechanism for obtaining such a pattern may be similar to though certainly not identical with the process involved in caloric habituation This, however, will be further discussed in a *paper in preparation (Forssman, 1963).*

ZUSAMMENFASSUNG

Fünfzehn Normalpersonen erhielten 12 aufeinanderfolgende kalorische Spülungen des rechten Ohres mit Wasser von 30°C Die Kalorisationen wurden bei vollem Licht vorgenommen, mit Ausnahme der ersten und zwölften Diese dienten als Tests um Vergleiche mit einer zuvor berichteten Serie von kalorischen Reizungen, alle bei Dunkelheit erfolgt, möglich zu machen Vier Qualitäten wurden verglichen (1) Augengeschwindigkeit, (2) Dauer des Nystagmus, (3) Laterotorsion und (4) Vertigo

Die Versuche zeigten den gleichen Umfang von Reaktionsverminderung bei Kalorisationen bei Licht wie bei Dunkelheit und auch die gleiche Reihenfolge der Reaktionsabnahme bei der Gewöhnung

Wenn das Licht eingeschaltet wurde, ergab sich eine plötzliche Abnahme, und wenn es abgeschaltet wurde, eine plötzliche Zunahme des Nystagmus und der Laterotorsion, aber nicht des Schwindelgefühles, das in gleicher Weise zurückging, unabhängig von Licht oder Dunkelheit Am Ende der Gewöhnungsversuche bei Licht war Laterotorsion oft die einzige erkennbare Wirkung der Kalorisation

Bei zunehmender Gewöhnung erhöhte sich die Dysrhythmie des Nystagmus mehr bei Licht als bei Dunkelheit

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University of Lund, Sweden

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APPENDIX

Light series

Values for maximum eye velocity, duration of nystagmus, maximum laterotorsion, maximum vertigo, and dysrhythmia of nystagmus from repeated calorizations of 15 normal subjects Every one received 12 consecutive irrigations with water of 30°C in the right ear The 1st and the 12th calorizations performed in darkness, all the others in full light *M* = mean value

TABLE 1 *Maximum eye velocity in °/sec*

Test subj no	Irrigation no											
	1	2	3	4	5	6	7	8	9	10	11	12
16	5 3	3 5	0	0	0	0	0	0	0	0	0	2 3
17	28 8	1 7	3 5	2 9	1 2	1 2	1 2	1 2	1 2	1 2	1 2	11 1
18	25 3	1 0	3 3	2 7	0	0	0	0	0	0	0	12 0
19	21 7	2 3	1 1	1 1	0	0	0	0	0	0	0	11 4
20	13 8	1 5	1 5	1 5	1 5	0	0	0	0	0	0	6 9
21	32 7	6 0	5 2	5 2	5 2	5 2	1 3	1 3	3 1	0	0	0
22	20 0	3 8	3 8	3 8	3 8	3 5	3 1	3 1	3 1	3 1	2 3	10 8
23	31 3	10 0	5 6	4 1	3 8	3 8	3 8	3 8	3 8	3 1	2 5	20 3
24	27 1	7 1	7 1	5 7	5 0	3 6	3 6	2 9	2 9	2 9	2 9	11 3
25	24 0	1 0	1 0	2 0	1 3	0	0	0	0	0	0	10 0
26	8 2	0	0	0	0	0	0	0	0	0	0	0 7
27	12 9	10 2	5 6	5 6	0	0	0	0	0	0	0	13 5
28	20 0	0	0	0	0	0	0	0	0	0	0	11 8
29	23 5	2 5	2 5	1 9	0	0	0	0	0	0	0	6 8
30	28 9	2 9	1 9	1 9	0	0	0	0	0	0	0	15 1
Σ	353 5	62 5	45 1	38 1	21 8	17 3	16 0	15 3	14 4	10 3	8 9	150 3
M	23 6	4 2	3 0	2 6	1 5	1 2	1 1	1 0	1 0	0 7	0 6	10 4

TABLE 2 *Duration of nystagmus in seconds*

Test subj no	Irrigation no 1	2	3	4	5	6	7	8	9	10	11	12
16	194	[illegible]	0	0	0	0	0	0	0	0	0	—
17	212	103	103	109	104	80	81	—	0	[illegible]	62	209
18	250	116	116	108	0	0	0	0	0	0	0	169
19	214	[illegible]	94	[illegible]	0	0	0	0	0	0	0	[illegible]
[illegible]	[illegible]	86	98	89	88	0	0	0	0	0	0	116
21	212	147	156	146	120	111	111	99	90	0	0	0
[illegible]	[illegible]	138	134	132	130	113	115	96	115	112	87	237
[illegible]3	296	188	189	150	151	149	150	150	[illegible]	122	126	232
[illegible]	[illegible]	[illegible]	[illegible]	134	123	120	108	116	[illegible]	101	103	204
[illegible]	204	[illegible]	100	100	[illegible]	0	0	0	0	0	0	167
[illegible]	209	0	0	0	0	0	0	0	0	0	0	172
[illegible]	[illegible]	[illegible]	[illegible]	99	0	0	0	0	0	0	0	154
[illegible]	[illegible]	0	0	0	0	0	0	0	0	0	0	214
[illegible]	[illegible]	118	118	112	0	0	0	0	0	0	0	161
[illegible]	[illegible]	89	[illegible]	90	0	0	0	0	0	0	0	203
Σ	[illegible]	[illegible]	1423	[illegible]	808	[illegible]	[illegible]	461	530	407	378	2411
M	233	10	[illegible]	91	51	38	38	33	[illegible]	[illegible]	[illegible]	172

TABLE 3 *Maximum laterotorsion in grammes*

Test subj no	Irrigation no 1	2	3	4	5	6	7	8	9	10	11	12
16	348	[illegible]	[illegible]	58	0	58	0	116	58	[illegible]	0	406
[illegible]	[illegible]	[illegible]	580	580	318	348	174	116	348	232	[illegible]	[illegible]
18	116	[illegible]	0	58	0	0	0	0	0	0	0	0
19	464	580	1044	812	696	812	580	464	580	348	348	406
[illegible]	[illegible]	[illegible]	[illegible]	348	348	[illegible]	406	0	58	116	116	812
[illegible]	0	[illegible]	[illegible]	464	290	[illegible]	174	116	116	174	232	0
[illegible]	[illegible]	348	[illegible]	[illegible]	[illegible]	464	290	[illegible]	232	464	116	580
24	[illegible]	580	[illegible]	[illegible]	23	116	58	116	116	116	58	406
[illegible]	58	464	[illegible]	[illegible]	290	[illegible]	[illegible]	290	116	[illegible]	116	696
[illegible]	464	[illegible]	[illegible]	[illegible]	290	348	[illegible]	232	174	290	232	348
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	452	[illegible]	[illegible]	339	[illegible]	[illegible]	509	452
[illegible]	[illegible]	292	[illegible]	511	511	[illegible]	438	[illegible]	292	219	219	402
[illegible]	[illegible]	584	511	511	511	584	[illegible]	511	365	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	0	[illegible]	91	[illegible]	[illegible]	0	3	110	[illegible]	110	146
[illegible]	[illegible]	[illegible]	[illegible]	438	[illegible]	[illegible]	438	[illegible]	365	[illegible]	511	584
Σ	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	5313	[illegible]	[illegible]	[illegible]	3463	3033	[illegible]
M	[illegible]	[illegible]	[illegible]	[illegible]	303	[illegible]	[illegible]	[illegible]	[illegible]	231	[illegible]	413

APPENDIX

Light series

Values for maximum eye-velocity, duration of nystagmus, maximum laterotorsion, maximum vertigo, and dysrhythmia of nystagmus from repeated calorizations of 15 normal subjects Every one received 12 consecutive irrigations with water of 30°C in the right ear The 1st and the 12th calorizations performed in darkness, all the others in full light M = mean value.

TABLE 1 *Maximum eye-velocity in °/sec*

Test subj no	Irrigation no											
	1	2	3	4	5	6	7	8	9	10	11	12
16	5 3	3 5	0	0	0	0	0	0	0	0	0	2 3
17	28 8	1 7	3 5	2 9	1 2	1 2	1 2	1 2	1 2	1 2	1 2	14 1
18	25 3	4 0	3 3	2 7	0	0	0	0	0	0	0	12 0
19	21 7	2 3	1 1	1 1	0	0	0	0	0	0	0	11 4
20	13 8	1 5	1 5	1 5	1 5	0	0	0	0	0	0	6 9
21	32 7	6 0	5 2	5 2	5 2	5 2	4 3	4 3	3 4	0	0	0
22	20 0	3 8	3 8	3 8	3 8	3 5	3 1	3 1	3 1	3 1	2 3	10 8
23	31 3	10 0	5 6	4 1	3 8	3 8	3 8	3 8	3 8	3 1	2 5	26 3
24	27 1	7 1	7 1	5 7	5 0	3 6	3 6	2 9	2 9	2 9	2 9	11 3
25	24 0	4 0	1 0	2 0	1 3	0	0	0	0	0	0	10 0
26	8 2	0	0	0	0	0	0	0	0	0	0	0 7
27	42 9	10 2	5 6	5 6	0	0	0	0	0	0	0	13 5
28	20 0	0	0	0	0	0	0	0	0	0	0	11 8
29	23 5	2 5	2 5	1 9	0	0	0	0	0	0	0	6 8
30	28 9	2 9	1 9	1 9	0	0	0	0	0	0	0	15 4
Σ	353 5	62 5	45 1	38 4	21 8	17 3	16 0	15 3	11 4	10 3	8 9	156 3
M	23 6	4 2	3 0	2 6	1 5	1 2	1 1	1 0	1 0	0 7	0 6	10 4

RETROGRADE JUGULAROGRAPHY IN THE DIAGNOSIS OF ABNORMALITIES OF THE SUPERIOR BULB OF THE INTERNAL JUGULAR VEIN

TOMAS GEJROT
Stockholm, Sweden

From the Department of Otolaryngology (Head Prof C.-A. Hamberger, M.D.), Karolinska Sjukhuset, Stockholm

Two cases of upward displacement of the superior bulb of the internal jugular vein are reported. In one case a pulsating vein was seen through the tympanic membrane, and in the other haemorrhage at paracentesis suggested the presence of the abnormality. The anatomical variation in the vein was confirmed by phlebography, using the technique evolved by the author (retrograde jugularography).

Displacement of the jugular vein upward into the middle ear is an anatomical variation which is of importance and interest to the otologist. This abnormality may give rise to clinical symptoms such as impaired hearing, tinnitus and vertigo. When the jugular vein is displaced paracentesis and other operations on the tympanic membrane and middle ear may involve special risks. Surgeons have always to pay particular attention to the possibility of variations in the course of the sigmoid sinus when performing mastoidectomy. According to the literature upward displacement of the sigmoid sinus has often been an incidental finding at an operation on the mastoid process and may result in undue haemorrhage during the operation.

It has been reported that abnormality of the superior bulb of the internal jugular vein is one of the causes of haemorrhage at myringotomy, particularly in textbooks this point has been stressed. Page (1914) was one of the first to describe this. He reported a case of thrombosis of the bulb of the jugular vein due to a lesion of the bulb which was displaced upward. At paracentesis of the tympanic membrane, which was found to be dark blue, severe haemorrhage occurred which could not be controlled otherwise than by tamponade of the auditory canal. On the following day mastoiditis supervened, resulting in thrombosis of the sinus.

Uffenorde wrote in his textbook that before 1942 only 10 cases of haemorrhage at paracentesis had been reported in which it had been possible to prove that the cause of the haemorrhage was upward displacement of the bulb. In the past few years two examples of upward displacement of the bulb were encountered at the Department of Otolaryngology [illegible]

[illegible] jugular vein retrograde jugularography established the diagnosis.

TABLE 4 *Maximum vertigo in degrees of vertigo*

Test subj no	Irrigation no											
	1	2	3	4	5	6	7	8	9	10	11	12
16	0	0	0	0	0	0	0	0	0	0	0	0
17	2	0	1	0	0	0	1	0	0	0	0	0
18	1	1	0	0	0	0	0	0	0	0	0	0
19	4	1	1	0	0	0	0	0	0	0	0	0
20	0	0	0	0	0	0	0	0	0	0	0	0
21	4	2	1	1	1	0	0	0	0	0	0	0
22	0	3	0	0	0	0	0	0	0	0	0	0
23	5	4	4	3	1	1	1	1	1	0	0	4
24	4	3	2	2	2	1	0	0	0	0	0	0
25	5	2	2	2	1	0	1	1	0	0	0	2
26	4	0	0	0	0	0	0	0	0	0	0	0
27	5	3	2	1	0	0	0	0	0	0	0	0
28	4	4	2	2	1	1	1	1	1	0	0	0
29	4	3	3	2	2	1	1	1	1	1	1	2
30	4	4	2	2	2	1	1	1	0	0	0	0
Σ	46	30	20	15	10	5	6	5	3	1	1	8
M	3 1	2 0	1 3	1 0	0 7	0 3	0 4	0 3	0 2	0 1	0 1	0 5

TABLE 5 *Dysrhythmia of nystagmus in grades of dysrhythmia*

Test subj no	Irrigation no												Σ
	1	2	3	4	5	6	7	8	9	10	11	12	
16	0	2	4	4	4	4	4	4	4	4	4	2	40
17	0	0	0	0	0	0	0	0	0	0	0	0	0
18	0	0	1	1	4	4	4	4	4	4	4	0	30
19	0	0	0	0	4	4	4	4	4	4	4	0	28
20	0	0	0	0	0	4	4	4	4	4	4	0	24
21	0	0	0	0	0	1	1	1	1	4	4	4	16
22	0	0	1	1	1	1	2	2	2	2	3	0	15
23	0	0	0	1	1	1	1	1	1	1	1	0	8
24	0	0	0	0	1	2	2	2	2	2	2	0	13
25	0	1	2	2	3	4	4	4	4	4	4	1	33
26	0	4	4	4	4	4	4	4	4	4	4	3	43
27	1	3	3	3	4	4	4	4	4	4	4	1	39
28	0	4	4	4	4	4	4	4	4	4	4	0	40
29	0	0	1	2	4	4	4	4	4	4	4	0	31
30	0	0	1	2	4	4	4	4	4	4	4	1	32
Σ	1	14	21	24	38	45	46	46	46	49	50	12	392

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Two cases of upward displacement of the superior bulb of the internal jugular vein are reported. In one case a pulsating vein was seen through the tympanic membrane, and in the other haemorrhage at paracentesis suggested the presence of the abnormality. The anatomical variation in the vein was confirmed by phlebography using the technique evolved by the author (retrograde jugulography).

Displacement of the jugular vein upward into the middle ear is an anatomical variation which is of importance and interest to the otologist. This abnormality may give rise to clinical symptoms such as impaired hearing, tinnitus and vertigo. When the jugular vein is displaced paracentesis and other operations on the tympanic membrane and middle ear may involve special risks. Surgeons have always to pay particular attention to the possibility of variations in the course of the sigmoid sinus when performing mastoidectomy. According to the literature upward displacement of the sigmoid sinus has often been an incidental finding at an operation on the mastoid process and may result in undue haemorrhage during the operation.

It has been reported that abnormality of the superior bulb of the internal jugular vein is one of the causes of haemorrhage at myringotomy, particularly in textbooks this point has been stressed. Page (1914) was one of the first to describe this. He reported a case of thrombosis of the bulb of the jugular vein due to a lesion of the bulb which was displaced upward. At paracentesis of the tympanic membrane, which was found to be dark blue, severe haemorrhage occurred which could not be controlled otherwise than by tamponade of the auditory canal. On the following day mastoiditis supervened, resulting in thrombosis of the sinus.

Uffenorde wrote in his textbook that before 1942 only 10 cases of haemorrhage at paracentesis had been reported in which it had been possible to prove that the cause of the haemorrhage was upward displacement of the bulb. In the past few years two examples of upward displacement of the bulb were encountered at the Department of Otolaryngology of this hospital. In one case haemorrhage occurred at paracentesis and in the other the bulb was visible through the tympanic membrane. Explorative tympanotomy and a special form of phlebography of the internal jugular vein, retrograde jugulography, established the diagnosis.

TABLE 4 *Maximum vertigo in degrees of vertigo*

Test subj no	Irrigation no 1	2	3	4	5	6	7	8	9	10	11	12
16	0	0	0	0	0	0	0	0	0	0	0	0
17	2	0	1	0	0	0	1	0	0	0	0	0
18	1	1	0	0	0	0	0	0	0	0	0	0
19	4	1	1	0	0	0	0	0	0	0	0	0
20	0	0	0	0	0	0	0	0	0	0	0	0
21	4	2	1	1	1	0	0	0	0	0	0	0
22	0	3	0	0	0	0	0	0	0	0	0	0
23	5	4	4	3	1	1	1	1	1	0	0	4
24	4	3	2	2	2	1	0	0	0	0	0	0
25	5	2	2	2	1	0	1	1	0	0	0	2
26	4	0	0	0	0	0	0	0	0	0	0	0
27	5	3	2	1	0	0	0	0	0	0	0	0
28	4	4	2	2	1	1	1	1	1	0	0	0
29	1	3	3	2	2	1	1	1	1	1	1	2
30	4	4	2	2	2	1	1	1	0	0	0	0
Σ	46	30	20	15	10	5	6	5	3	1	1	8
M	3 1	2 0	1 3	1 0	0 7	0 3	0 4	0 3	0 2	0 1	0 1	0 5

TABLE 5 *Dysrhythmia of nystagmus in grades of dysrhythmia*

Test subj no	Irrigation no 1	2	3	4	5	6	7	8	9	10	11	12	Σ
16	0	2	4	4	4	1	4	1	4	4	4	2	40
17	0	0	0	0	0	0	0	0	0	0	0	0	0
18	0	0	1	1	4	4	1	1	4	1	4	0	31
19	0	0	0	0	1	4	4	4	1	1	1	0	28
20	0	0	0	0	0	1	4	4	4	4	1	0	24
21	0	0	0	0	0	1	1	1	1	4	1	4	16
22	0	0	1	1	1	1	2	2	2	2	3	0	15
23	0	0	0	1	1	1	1	1	1	1	1	0	8
24	0	0	0	0	1	2	2	2	2	2	2	0	13
25	0	1	2	2	3	4	4	1	4	1	1	1	33
26	0	1	4	4	4	4	4	4	1	1	1	3	43
27	1	3	3	3	4	4	4	1	4	1	1	1	39
28	0	1	4	1	4	1	1	1	1	4	4	0	40
29	0	0	1	2	4	4	1	1	1	1	1	0	31
30	0	0	1	2	4	4	1	1	1	4	1	1	32
Σ	1	14	21	24	38	45	46	46	46	49	50	12	392

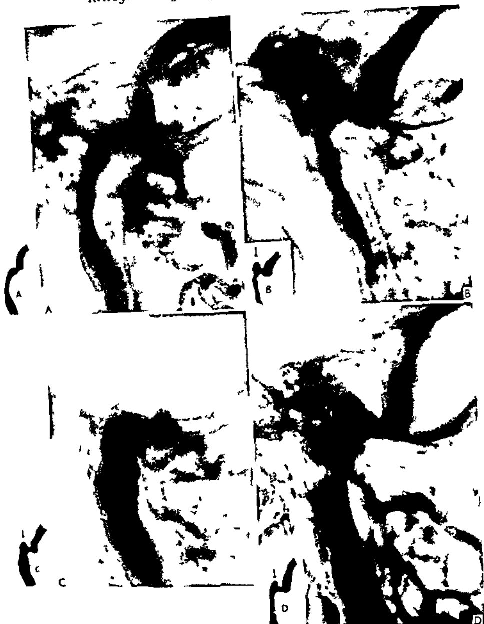


Fig. 1. Lateral retrograde jugularograms. A Normal appearance of the vein. *B* Dehiscence of the superior bulb in a 10 years old boy with blue eardrum (Case 1). C Dehiscence of a superior bulb in a 4[illegible] years old woman. The pulsating bulb could be seen at otoscopic examination (Case 2). *D* Asymptomatic upward displacement of the superior bulb of the internal jugular vein.

It is interesting to note that the abnormal bulb was on the right side in all except one of the cases reported here. This observation is in good agreement with the anatomical observation that the transverse sinus and the jugular

Technique of retrograde jugularography

The internal jugular vein is punctured in the neck and a catheter is inserted by the method of Seldinger (1953) as far up as the bulb. Contrast medium is then injected in retrograde direction applying maximum manual pressure and with the vein compressed distally on the neck. This technique results in visualization of tissues such as the sigmoid sinus and the bulb of the internal jugular vein (Gejrot & Lindbom 1960).

Case reports

Case 1

The patient, a boy aged 10 years, had been unsuccessfully treated for symptoms of secretory middle ear disease for several months. The tympanic membrane was seen to be dark blue in the posterior lower quadrant. There was pulsating tinnitus and impaired conductive hearing in the right ear. At paracentesis severe haemorrhage occurred which was controlled by tamponing the auditory canal. The post-operative course was uneventful. Roentgen examination of the ear and skull showed a small pneumatized area and the jugular foramen to be considerably wider than normal on the affected side. Retrograde jugularography disclosed that the superior bulb was much higher up than normal and bulged into the middle ear (Fig. 1B). At operation the bulb was seen to protrude like a large pulsating vein and to lie close to the tympanic membrane, only loose adhesions separating it from the latter.

Case 2

The patient, a woman aged 45 years, had a radical operation for mastoiditis of the left ear in 1936. Twenty-four years later there was a discharge from the right ear with tinnitus, slight dizziness and spontaneous nystagmus to the left. Otoscopic examination disclosed a pulsating bulb on the inner side of the tympanic membrane which showed a central perforation. Compression of the vein of the neck on the right side was followed by an increase in the nystagmus whilst the pulsations disappeared. Retrograde jugularography confirmed marked upward displacement of the bulb.

DISCUSSION

The causes of haemorrhage at paracentesis are manifold. Apart from abnormalities of the bulb, varices of the tympanic membrane, haemorrhagic exudate, vascular tumours such as glomus tympanicum and accessory veins may account for the complication. As abnormalities of the bulb do not invariably give rise to symptoms they are rarely encountered in clinical practice but are fairly common post-mortem findings (Haslam 1914). A moderately or markedly enlarged bulb which had not caused any symptoms was an incidental finding in three cases out of 80 patients examined by jugularography in this hospital.

ENCEPHALOMENINGOCELE IN THE FRONTAL SINUS

Borje Drettner
Uppsala Sweden

From the Department of Otolaryngology (Head Prof A Sjoberg M D)
University of Uppsala

A case with herniation of the anterior horn of the left lateral ventricle through the posterior wall of the left frontal sinus is described The encephalo meningocele which was operated on had developed in adult years as a result of an aqueduct stenosis with internal hydrocephalus

Encephalomeningoceles may be classified into three groups according to their localization occipital sincipital and basal The last two groups are those that are of main interest in otology The different types of encephalo meningocele belonging to these two groups are shown in Table 1 according to the classification made by v Meyer (1890) Safranek (1926) and Gisselsson (1947) The latter author traced altogether 24 cases of intranasal encephalomeningocele published in the literature he also described one case of his own In the majority of cases the encephalomeningocele had been diagnosed originally as an ordinary nasal polypus and had been removed often with meningitis as a result

In none of the cases referred to by Gisselsson was the encephalomeningo

Table 1 *Classification of sincipital and basal encephalomeningoceles*

	Hernial aperture	Localization
Sincipital		
E nasofrontalis	Oss frontale nasale	Glabella
E nasoethmoidalis	Oss frontale nasale-ethmoidale	Anterior edge of os nasale
E nasoorbitalis	Oss frontale ethmoidale lacrimale	Medial corner of the eye or frontal part of the orbit
Basal		
E sphenopharyngea	Os sphenoidale	Epipharynx
E sphenoethmoidalis	Oss sphenoidale ethmoidale	Posterior part of nasal cavity or in epipharynx
E transethmoidalis s intranasalis	Lamina cribrosa	Intranasal
E sphenoorbitalis	Fissura orb sup	Behind the eye
E sphenomaxillaris	Fissura orb sup	Fossa sphenomaxillaris via fissura orb inf

vein are generally larger on the right side than on the left, according to many authors in 75 per cent of cases (*Koerner, 1886, Edwards, 1931, Frenckner 1940*). The jugular foramen is also larger on the side of the affected bulb. It has also been reported that the sigmoid sinus and the superior bulb of the internal jugular vein tend to lie closer to the auditory canal on the right side (Ersner & Myers, 1933).

In case 2, the patient had an operation on the opposite ear elsewhere 21 years previously. She had probably developed thrombosis of the sinus post operatively (the hospital records of the patient were not available) because angiography of the carotid artery revealed insufficiency of the left sinus. It was not possible to perform jugularography on the left side. Queckenstedt's test *failed to produce a rise in the pressure of the cerebro spinal fluid following* compression of the left cervical vein. As the radiographs taken in 1936 were not available for comparison it can only be assumed that increased blood flow on the right side accounted for dilatation of the jugular foramen and upward displacement of the bulb.

ZUSAMMENFASSUNG

Zwei Fälle mit sogenanntem Bulbushochstand mit Dehiszenz, bei denen die häutige Wand ohne Knochenbedeckung durch den Boden der Pauke vorwölbt, sind beschrieben. In einem Falle war es möglich, den Bulbus durch das Trommelfell zu sehen. In dem anderen Falle hat man bei Parazentese den Bulbus angeritzt und eine Blutung bekommen. Der Verfasser hat diese Anomalie mit einer speziellen Phlebographie, retrograder Jugularographie, illustriert.

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Dept. of Otolaryngology, Karolinska Hospital, Stockholm, Sweden

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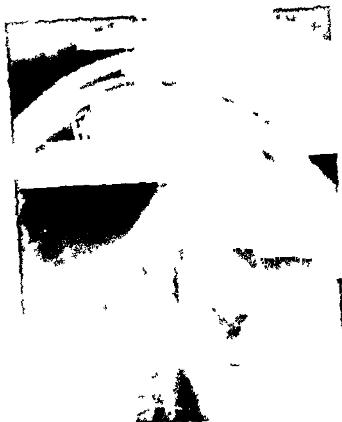


Fig. 2. Roentgen examination of the sinuses 1962. Opacity in the left frontal sinus and polypus-like mucosal swelling at the bottom of the right maxillary sinus.

Case History

The patient was a 31-year-old pipe fitter, who in 1954 and 1955 was examined roentgenologically because of acute maxillary sinusitis. The frontal sinuses appeared completely normal in the roentgen pictures on both occasions (Fig. 1). Since about 1955 he had suffered from short attacks of pain around the left frontal sinus on lifting heavy articles or straining at stools. These symptoms were most pronounced when he had a cold. During the summer of 1961 he had a transient attack of unconsciousness with general cramp while visiting a place of work where there were toxic gases. In the autumn of 1961 the patient suffered for about two months with paraesthesia on the left side of the face. At the same time he had a prolonged respiratory infection and roentgen examination showed opacity of the left frontal sinus and an enlarged sella turcica. Two encephalographies were performed at his local hospital, and on both occasions the basal cisterns were filled with air but no air was seen in the ventricular system.

At the beginning of 1962 the patient was admitted to the Otological Clinic



Fig 1 Roentgen examination of the sinuses 1955 Mucosal swelling in the right maxillary sinus, with normal frontal sinuses

cele localized to the frontal sinus Only two cases have been found in the literature with an encephalomeningocele at this site These cases (Lecuire *et al*, 1959, Maduro *et al*, 1961) were diagnosed as being due to cranial trauma One had a discharge of liquor from one nostril 16 years after the trauma and the other had meningitis 8 years after the accident Operations with neuro surgical approach were performed and in both cases an opening was found in the dura corresponding to the posterior wall of the left frontal sinus, with a cerebral hernia passing through the opening The hernias were removed and the dural defects were covered with fascia lata There were no subsequent complications in either of the two cases

A new case of encephalomeningocele in the frontal sinus deserves reporting partly because its localization is rare but worthy of notice and partly because in this particular case the encephalomeningocele had an unusual mode of origin



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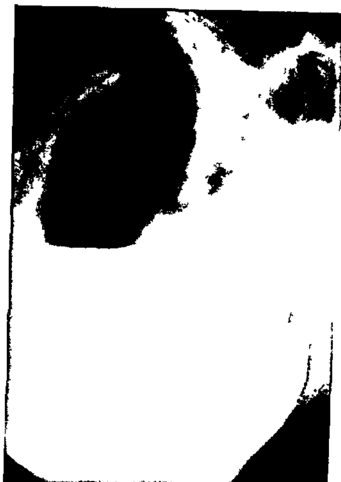


Fig. 3. Ventriculography. The widened anterior horn of the left lateral ventricle has an offshoot towards the left frontal sinus, in the posterior wall of which two clips can be seen.

of the Uppsala University Hospital with a diagnosis of mucocele in the left frontal sinus. The configuration of the skull and face were normal, and palpation of the areas around the frontal sinuses revealed nothing pathological. Rhinoscopy, eye status, nerve status and EEG were normal. Roentgen examination of the sinuses revealed that the left frontal sinus was opaque, and also showed a polypus-like mucosal thickening in the bottom of the right maxillary sinus (Fig. 2). No destruction of the frontal sinus walls was revealed by tomography. On roentgen examination of the skull pronounced digital impressions were seen and also enlargement of the sella turcica with atrophy of the posterior wall. Further encephalography showed that the lobes of the cerebellum were curved below at a level with the arch of the atlas, but no air passed upwards into the ventricular system. Lumbar oxygen myelography gave normal results. On vertebral angiography it was found that the vessels in the posterior skull cavity were extended and dislocated basally as with dilatation of the lateral ventricles. The roentgenological findings were interpreted as stenosis of the aqueduct of Sylvius + Arnold-Chiari malformation + mucocele in the left frontal sinus.

Because of the latter diagnosis it was decided to explore the left frontal



Fig. 4. Tomography of the frontal sinuses. Rounded bone defect in the posterior wall of the left frontal sinus, with two clips in the defect.

sinus, which was opened externally under local anaesthesia. The base and anterior wall of the frontal sinus were intact. In the frontal sinus a sac-like formation the size of a plum was found; this was opened and a teaspoonful of white viscous material was withdrawn. When part of the sac had been removed it was found that it continued with a narrow hernial neck through a pencil-wide defect in the posterior wall of the frontal sinus into the frontal skull cavity. On straining a profuse amount of liquor emptied from the sac which was actually an encephalomeningocele. The frontal sinus mucosa and the meningocele sac were freed towards the opening in the posterior wall. In these soft parts a detached piece of bone was found, which was flat and of approximately the same size as the opening in the posterior wall of the frontal sinus. The hernial neck was closed with two clips, and gel foam was placed over the opening in the posterior wall of the frontal sinus. The patient appeared unaffected during the operation. He was subsequently given large doses of antibiotics.

Microscopical examination confirmed the diagnosis of encephalomeningocele. The bone fragment was coated on one side with respiratory tract mucosa.

The day after the operation the patient had right-sided cramp, which was quickly relieved by an injection of phenemal. He was transferred to the neurosurgical clinic of the Seraphim Hospital, Stockholm. Two weeks after the frontal sinus operation ventriculography was performed and showed that

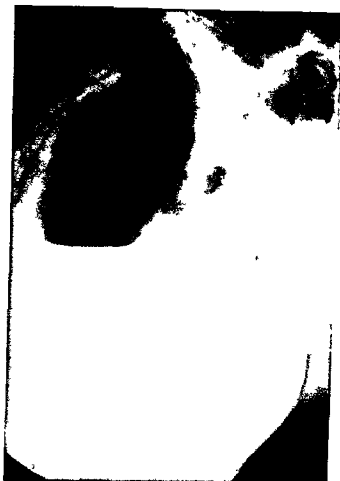


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both lateral ventricles were considerably widened and extended to a distan[ce]
of 2 cm from the internal lateral parietal table. The left anterior horn had [an]
offshoot towards the posterior wall of the left frontal sinus (Fig. 3). The thi[rd]
ventricle was enlarged. In the centre of the aqueduct there was total passa[ge]
obstruction with a rounded end. On the diagnosis of Arnold Chiari m[al]formation and aqueduct stenosis a ventriculo cisternostomy was perform[ed]
according to the method of Torkildsen and the subsequent course was fr[ee]
of complications.

At a follow up examination six months after the operation the patient w[as]
completely free of symptoms and capable of working as a pipe fitter. T[he]
eye status and neurological examination results were normal. The l[eft]
frontal sinus was found on roentgen examination to have normal air conte[nt].
Tomography revealed the defect in the posterior wall of the frontal sinus a[nd]
in this opening the clips were seen (Fig. 4).

Summary

A case is reported of a 31 year old man who in 1955 had roentgenological[ly]
normal frontal sinuses and who since that time has had pain around the le[ft]
frontal sinus on lifting or straining. Roentgen examination in 1962 show[ed]
opacity of the left frontal sinus and also signs of stenosis in the aqueduct [of]
Sylvius. The left frontal sinus was explored and an encephalomeningoce[le]
passing through a pencil wide opening in the posterior wall of the front[al]
sinus was found and removed. A small detached bone fragment was al[so]
found in the frontal sinus. Ventriculography two weeks after the operati[on]
showed aqueduct stenosis with widened lateral ventricles; the left anteri[or]
horn had an anterior offshoot from which the encephalomeningocele in th[e]
left frontal sinus had arisen. Ventriculo cisternostomy according to Torkil[d]sen was performed in the neuro surgical clinic. At a follow up examinatio[n]
six months after the operation the patient was completely free of symptom[s].

DISCUSSION

The encephalomeningocele in this case cannot have been congenital since the frontal sinuses were roentgenologically normal before the condition was manifest. The case history supports the view that the encephalomeningocele occurred some time during the period between 1955 and 1962 as a herniation of the anterior horn of the left lateral ventricle through the posterior wall of the frontal sinus. Whether there was a pre formed defect in the posterior wall or whether the fragment of bone lying detached in the frontal sinus constituted part of the posterior wall of the frontal sinus that had been removed by pressure from the hernial sac is impossible to decide. The agreement in size between the defect and the fragment and the mucosal coating on one side of the fragment appear to support the latter hypothesis.

Since in spite of pronounced internal hydrocephalus the shape of the

patient's head was normal it is probable that the aqueduct stenosis did not occur until after the closing of the sutures between the bones of the skull and that the encephalomeningocele was formed secondarily through increased intraventricular pressure

The opacity in the left frontal sinus was diagnosed pre operatively as a mucocele although the symptom picture was somewhat atypical The incorrect diagnosis was due to the presence of other roentgenological signs of inflammation in the accessory sinuses through mucosal swelling in a maxillary sinus and also to the fact that the patient had had previous clinical signs of acute sinusitis

The pain of which the patient complained on lifting and straining was probably caused by a temporary rise in pressure in the encephalomeningocele or by the consequent pressure change in the frontal sinus Such symptoms do not usually occur with a frontal sinus mucocele It is possible that if roentgen examination had been carried out while the patient was straining or during cervical venous stasis this might have revealed increased opacity or increased extent of the density in the frontal sinus and thus could have further supported a diagnosis of encephalomeningocele and contradicted that of a mucocele An examination such as this should be considered in cases with atypical opacity in the frontal sinus where encephalomeningocele is a conceivable diagnosis

ZUSAMMENFASSUNG

Ein Fall von Hernienbildung des linken Seitenventrikel Vorderhornes durch die linke Stirnhöhlenhinterwand wird beschrieben Die Encephalomeningozele die operiert worden ist hatte sich erst im Erwachsenenalter als Folge einer Aquaeductusstenose mit Hydrocephalus internus entwickelt

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Department of Otolaryngology
University of Uppsala Sweden

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MEASUREMENT OF TONE RESPONSE BY THE HUMAN FOETUS[1]

A preliminary report

BERTIL JOHANSSON, ERIK WEDENBERG and BJÖRN WESTIN
Stockholm, Sweden

From the Department of Technical Audiology, Karolinska Institutet, the Department of Oto-Laryngology, Karolinska Hospital and the Department of Obstetrics and Gynecology, Sabbatsberg Hospital

It has earlier been shown that the newborn reacts to acoustical stimuli and that audiometric measurements can be carried out on them (Wedenberg 1956, 1963). By about the 24th week of intrauterine life the cochlea and the sensory end organ have reached their normal development (Ormerod, 1960; Bast, 1949). Measurements on *prematures* born at 27–28 weeks indicated that the *foetus* at this age reacted to an acoustical stimulus by a change in the pulse rate (Wedenberg, Westin, 1958, unpublished data). Such reactions by the foetus have recently been reported (Murphy, 1962; Fleischer, 1955). At frequencies below 1500 Hz the tactile stimulus is not negligible. As far as an adult's reaction is concerned, frequencies above 1500 Hz must be used to exclude the possibility that the reaction is to vibration (Knudsen, 1928).

The equipment and procedure for this investigation will be described in detail in the final report. The arrangements for calibrating of the system are shown in Fig. 1. The whole surface of the vibrator is placed in close contact with the body of the subject and a microphone is inserted in the uterus.

By means of the bars A, B and C the distance between the microphone and the vibrator has been calculated. For a distance of about 10 cm the sound pressure level at 3000 Hz was 110 ± 6 db, limits obtained on four subjects. A typical frequency response curve is shown in Fig. 2.

Mothers with 2–7 weeks to term were selected for the investigation. The mother was placed on a bed with her head lowered to minimize circulatory disturbance due to the supine position. In spite of this, fainting attacks occurred in some cases. The position of the head of the foetus was determined and the decided position of the vibrator was marked on the skin. The microphone of a phono cardiograph was placed where the beats of the foetal heart were best heard (Fig. 3). The subject was asked to relax.

After a rest of 5–10 min the control measurements were started. These included a recording of the beats of the foetal heart without stimulation. A sharp clap behind the mother's head, the application of the vibrator and a broad band masking noise applied to both ears of the mother did not interfere with the reaction of the foetus.

[1] This investigation was supported by research grants from The Swedish Medical Research Council, The Swedish Technical Research Council, The Association for the Aid of Crippled Children, The Association "Solstickan".

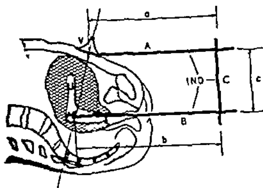


Fig. 1 Calibration set up V, vibrator, sound source, *M*, microphone cartridge, *IND*, position indicator U, uterus

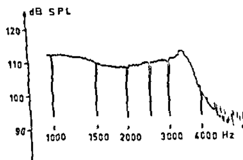


Fig. 2 Frequency response curve from a woman who has just given birth

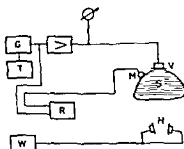


Fig. 3 Block diagram for measurements of tone response by the foetus G, pure tone oscillator; *T* timer *R* phono-cardiograph W white noise generator, V, vibrator, sound source, *M*, microphone S subject *H* headphones for masking noise

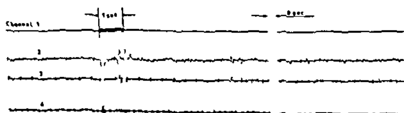


Fig. 4 Recording of the reaction of the foetus to a tone of 3000 Hz, 110 db SPL *for* 1 sec
three different bands Case 3, 2nd series A general muscu-

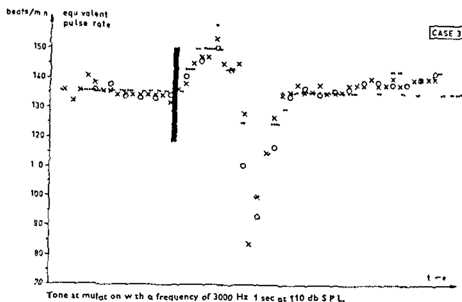


FIG 5 The reaction of total pulse rate to the tone, indicated by the vertical thick line plotted against time , Equivalent pulse rate, beats/min every beat indicated ×, equivalent pulse rate beats/min, integrated over three beats ○, equivalent pulse rate, beats/min integrated over six beats Case 3, 2nd series

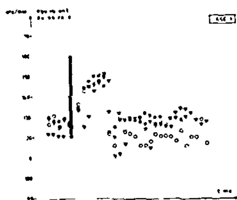
Tone stimulation with a frequency of 3000 Hz, 1 sec at 110 db S P L

Tone stimulation with a frequency of 3000 Hz, 1 sec at 110 db S P L

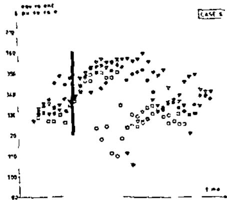
Tone stimulation with a frequency of 3000 Hz 1 sec at 110 db S P L

Tone stimulation with a frequency of 3000 Hz 1 sec at 110 db S P L

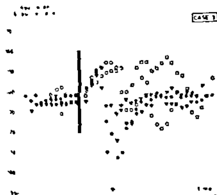
FIG 6 The reaction of the foetus to the tone, indicated by thick vertical lines Equivalent pulse rate of 10 foetuses (beats per minute) integrated over six beats ○, *first series* ▽, *second series* ●, third series ▼, fourth series □, fifth series



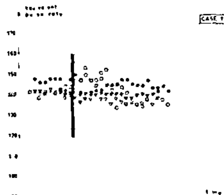
Tone stimulation with a frequency of 3000 Hz,
1 sec at 110 db S P L



Tone stimulation with a frequency of 3000 Hz,
1 sec at 110 db S P L



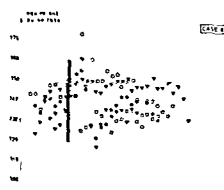
Tone stimulation with a frequency of 3000 Hz,
1 sec at 110 db S P L



Tone stimulation with a frequency of 3000 Hz,
1 sec at 110 db S P L



Tone stimulation with a frequency of 3000 Hz,
1 sec at 110 db S P L



Tone stimulation with a frequency of 3000 Hz,
1 sec at 110 db S P L

Fig 7

By means of a timer unit, *T* in Fig. 3, a pure tone of 3000 Hz was presented for 1 sec at a sound pressure level of 110 db. At a frequency of 3000 Hz a vibratory sensation at the skin of an adult is excluded and this can also be assumed for the foetus. The pulse rate of the foetus was recorded with the phono cardiograph. Under the presumption that other reactions to the stimulus can be disregarded, a change in the pulse rate can be considered as a reaction of the auditory system.

In the phono cardiogram reproduced in Fig. 4 movements of the foetus are distinctly depicted, these correspond to direct observations.

In Fig. 5 the same recording is represented with different integrating periods. Integration over six beats was chosen.

Twelve foetuses were examined. Four or five tests were performed on all except no. 9, the second test for whom disclosed abnormal values before the tone was applied. This is obviously due to a vena cava syndrome with fainting attacks. Subject 2 was excluded because the head was too deep in the pelvis and subject 5 because arythmia was detected before the tests.

The remaining 10 foetuses are represented in Fig. 6 and 7. For each series the significance of the deviations in the pulse rate were checked by the *t*-test.

From 45 tests on 10 foetuses 35 showed a highly significant deviation $P < 0.001$, five tests $0.001 < P < 0.01$, two tests $0.01 < P < 0.05$ and only three non significant deviations of the increasing pulse rate.

Postnatal tests showed that the hearing of all the subjects was normal over the frequency range 500–4000 Hz.

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Dept. of Otolaryngology, Karolinska Sjukhuset, Stockholm 60, Sweden

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PROBLEMS CONCERNING THE BONE CONDUCTION TESTS

A. Laskiewicz
London, Great Britain

After limiting the air conduction threshold one bone conduction receiver is placed at the front of the tested person. Double contralateral masking: an olive of the rubber tube, connected with Bárány's box is tightly fitted to the external meatus and to the mastoid bone, is placed an oscillating vulcanite adapter connected with this box by a bifurcate metalic tube. Audiometric bone conducting tests are performed in the interrupted form eliminating the across head difference. Fifteen cases of different impairments of hearing, bone conduction Gellé, Wheatstone, Bing, Runge tests and the crossed hearing of bone perception in two cases of congenital deafness are discussed.

Testing the bone conduction by using a vibrating tuning fork and particularly the audiometer can be regarded as exact clinical method to measure the perceptive function of the entire auditory apparatus, i.e. the conducting mechanism of the middle ear, the sensitivity of the cochlea and the central acoustical pathways as well. When the vibrating tuning fork or the bone conducting receiver is applied to any part of the head one part of the pulsed tone passes directly to the perilymph of the inner ear while the other one sets the surrounding air into vibration creating air waves in the external meatus and the tympanic cavity, the so called secondary air waves (sekundärer Luftschall B. Langenbeck) which produces a pressure amplification of aerial sounds and increases greatly the sensitivity of the inner ear. Mader has proved (1900) that the sound waves even of a faint intensity set into vibration the bone tissue of the skull, the otic capsule and the perilymph of the cochlea not only on the one side but simultaneously the contralateral ear is influenced by the same pulsed tone, the base of the skull acting as conveyer of the bone conducted sound energy. The intensity and phase relations of the bone conducted tone depend on the compactness of the bones forming the base of the skull (Kessel, Frey). Since there it is evident that bone conduction acts mainly on the labyrinth walls at least at high frequency, the point which was experimentally proved by Bekesy in 1932.

The skull moves as a rigid body when excited by sinusoidal vibrations of a frequency below 800 cps. As the frequency rises the elasticity of the skull comes into play and the forehead as well as its occipital part vibrate in opposite directions. Above 1500 cps the skull vibrates in sections, the nodal points between them move in a uniform manner with the point of applied oscillator. Bekesy confirmed three types of bone conduction mechanisms: (a) Classical bone conduction computing the vibration of the head like

a bell inertia of the ossicular chain together with the inertia of the lower jaw (*b*) Skull bone conduction i e inertia of the ossicles together with compression of bone conduction as *compression alone independent* of both events mentioned under *a* and *b* the state of the middle ear and vibrations of the lower jaw The mechanism of the named conduction is dependent upon the existence of volume difference of both scalae of the cochlea and the difference of mobility of both windows In 1953 Zwislocki examined the phenomenon again and found that the *mode of vibration in the cochlea does* not depend on the mode of stimulation Miodonski described (1953) the *vibrating patterns of the cochlear spindle* (modiolus) (solenoid type mechanism) as a consequence of long lasting effect of high intensity tuning fork applied to the mastoid bone Kirikae and Naunton discuss the role of inertia of the inner ear mechanism as a third type of bone conduction the hearing by which is mediated by vibrations of the skin skull and the liquids contained within its cavities and the *inner ear Pressure of the receiver to the* skull and its position during testing are responsible for differences between *thresholds at different locations of receiver to the head* This variety seems to be more expressed at 500–1000 cps than at 2000–4000 cps Thresholds at low frequencies improve significantly as tension of the vibrator is augmented Fournier (1954) accepted that sound transmitted by bone has physical characteristics as air borne sound The lesions in the cochlea or within the acoustical *pathways rise the threshold of air conduction* but the degree of hearing loss depends on the kind and the localisation of the lesion and Onchi has shown that any alterations of *the middle ear rise the bone* conduction threshold to a certain degree Kietz in his audiometric studies has found 32 000 cps as a limit for measurement of bone conduction of the head He distinguishes two different kinds of nerve deafness One did not demonstrate any bone conduction of ultrasonic sounds above 16 000 cps The other was able to hear up to the 32 000 cps limit Bellucci has indicated the patterns of ultrasonic perception over the head being calculated from *25 000 to 62 500 cps provided that the vestibular function in the tested person* is unchanged In the normal subjects the tuning fork is heard about twice as long by air conduction as by bone conduction the intensity of which requires to be on an average of 40 db The intensity of 1000 cps sets all bones of the skull into vibration but the shorter stimulating sound waves cause one insignificant deformation only of those bones in the form of compression and decompression Bekesy pointed out the role of the jaw in bone conduction When the skull vibrates the mandible remains relatively stationary By this relative motion a compression and rarefaction of the air in the *external auditory meatus is produced* The increased bone conduction can be produced when the obstruction of the meatus is made applying the stopper *beyond the cartilaginous part of the canal* Franke Gierke Grossman and Western have demonstrated in the same condition and closed mouth that the perception of *bone conducted tuning forks rises by 6 10 db* at frequency from 10 700 cps Langenbeck states that at low frequencies the

pressure in the external auditory canal and the cochlea are in opposition. Inertia of the lower jaw results in depression in the right auditory canal and a pressure in the left auditory canal corresponding the pressure in the labyrinth itself and in converse manner. Each ear perceives a "labyrinth sound" and an "air sound", the latter being twice the intensity of the former. He estimates a delay of 0.2–0.4 ml sec between the "labyrinth sound" and the "air sound". As for the craniotympanal conduction the named authors agree that transmission of the sound waves to the inner ear is due mainly to the rhythmical movements and molecular oscillations of the stapes being also stimulated by its membrano-tendinous junction, which are set into vibration by the named waves. Perception of a vibrating fork depends not only on the intensity and the pitch of the given tone but also on the region where its base is placed on the skull. V. Urbantschitsch (1901) has pointed out that a vibrating tuning fork C_1–C_2 set above the upper part of the nose is lateralized usually to right ear while its moving few *mm* higher turns the sound perception towards the left side. In normal individuals the fork placed in the middle line of the skull (forehead or vertex) is perceived *in both ears* clearly but otherwise the tested person experienced this tone inside the head only. There are known cases of so called contralateral or *crossed localization* of the tested tone especially when the vibrating fork is placed on the tuber frontale. Similar to the named phenomenon is the *lateralization of the tested tone* by bone conduction. If this test is lateralized in the worse ear the bone conduction curve is generally lower than the bone *conduction threshold* of the better ear. Savart, Wallaston and E. H. Weber were the first observers who stated that applying a vibrating tuning fork C_1–C_2 *at the top of the head*, the tested person perceives the pulsating tone in the ear the external meatus of which was even slightly obstructed by a small quantity of *cerumen*. Mach (1864) explained this phenomenon that the sound in the labyrinth is prevented from escaping through the external canal and the subsequent sound waves add up together in the tympanic cavity. Toynbee accepted one increased resonance of the air within the middle ear and the external auditory canal the pressure of which on the *labyrinth* is responsible for the phenomenon in question (Lucae). Politzer in his textbook *Diseases of the Ear* (1892) joined the theory of *Mach and Toynbee*. The experimental investigations of M. A. [illegible] (1881) and especially those of *Betzold*, Brunings, Kranz and Sullivan draw attention to increased *tension* of the entire conducting apparatus due to increased *resonance* within the *middle and external ear*. Herzog and Barany described the inertial bone *conduction*. Boeninghaus and Lawrence have completed this theory accepting that *one part of the mollecular* oscillations transmitted through *the bones* of the skull besides the impaired or cancelled air conductions will *be* used to increase the named tension. Further investigations concerning the *role* of the conduction organs in perception of hearing through the bone transmission are connected with the names of Langenbeck, Hanke, Meyer z. *Gottesberge*, Schubert, Kley, Huizing, T. Palva, King, Arnold and Mehmke. The first pointed to the simultaneous

vibration of the air in the tympanic cavity and the external auditory canal. Kley and Mehmke state, using acoustical sounds, that the frequency and elevation of the named vibrations can only be proved until C_5 4096 cps. Mehmke has demonstrated experimentally that above the threshold of 2000 cps any lesion of the ossicles or diminished elasticity of its vibrations is associated with changes in the bone conduction tests. These factors come into consideration to explain the Carhart phenomenon in which break down of threshold of the bone conduction curve at frequencies from C_1 to C_3 and the intensity 5–15 db so called "Carhart notch" is very characteristic for stiffness of the ossicular chain and fixation of the stapedial footplate. Increased elasticity of the conducting apparatus in Gellé's test presents a bone conduction curve quite different from the shape of the "Carhart notch". The small differences in resonance frequently between the left and right ear of about 3 db really to exist and its components are of the same magnitude. It looks as if the air vibration force within the middle ear and pneumatic system of the temporal bone is rather stronger than the compression components along several nodal lines because of the lateralisation shift in the region of 3000 cps (Groen). There is a tendency in normal conditions to lateralize the tuning fork in one ear in the Weber test because of a slight anatomical difference between the two ears. This effect of lateralization can be achieved by (*a*) better sound conduction to one cochlea, (*b*) by a phase difference between the two sound waves entering both cochleae while the bone conducting tone is lateralized in the cochlea with the leading phase. The difference of 3 db between both ears is responsible for the named lateralization of tone. The value of the Weber test is to be considered from the point of its three categories. The type below the frequency of 1000 cps, the second one between 1000 and 3000 cps and the third above 3000 cps. The *difference between the bone conduction audiograms in patients with otosclerosis* and the normal lies mainly in the absence of inertia components giving raise to an average loss of 5 db at 500 cps, 10 db at 1000 cps, 15 at 2000 cps, 10 at 3000 cps and 5 at 4000 cps. The *bone conduction in otosclerosis* shows a progressive loss with increasing frequency because the scala tympani is blocked for the higher frequencies, the low frequency vibrations find some escape through the cochlear aqueduct. Only if the resonance frequencies have the same values for the right and the left ear the "Carhart notch" may appear to its full extent (Groen). The named author pointed out that the Weber test in fenestrated ears shows lateralization to the operated ear in the whole range. In many patients the lateralization in question shifted in the descant zone from the non operated to the operated ear in the course of two months, depending upon the natural frequencies of the ossicular chain and the air volume in both ears. After onesided stapedectomy the Weber test shows lateralization for 1000 cps, 2000 cps and 3000 cps in the non operated ear. When a slight trauma has been inflicted during stapedectomy or fenestration the Weber test will be lateralized to the operated ear presumably for the lower frequencies but as far as the higher ones are concerned

it is puzzling to state their lateralization in the non operated ear (Groen). The recovery from the slight trauma during the named operation would cause the lateralization to shift into the operated ear for the higher frequencies also.

I tested the bone conduction in 15 of my own cases, i.e. eight cases after relapsing catarrhal inflammations of the middle ear, three cases of otosclerosis, two of Menière's disease, one case after unilateral labyrinthitis and two cases of congenital deafness. I must emphasize that testing of the bone conduction in these cases was performed applying the method of Rainville modified by Lightfoot, Tillman, Kess, *Milburne, Hayes and T. Palva*. This method is the most reliable, precise and the most objective hearing tests in question. I tried at first to determine the loss of hearing for air conduction pure tones (speech, conversation, audiometric test) the threshold of which is very helpful for differential diagnosis. Masking of the contralateral ear was applied. Hallpike pointed out that a more perfect camera silenta would be able with greater certainty to prove that bone conduction is prolonged because the surrounding noise is abolished. Testing the bone conduction in an open room I found in one great number of examined cases the difference of 10–22 db as compared with the results obtained in camera silenta. Masking with narrow band noises inhibits usually at once responses to tones. It is indicated as peripheral in origin to inhibit mainly the high tones. The energy contained in any given band of the noise is concentrated upon a few endings in the basal region of the cochlea when the density of innervation is relatively great. For the lower tones, however, the same energy is more widely distributed. Dividing the energy of the tone by that *per cycle of the noise we come out with the* number of cycles over with the noise is effectively operating one. Fletcher supposed that the band in question represents the excitation of some constant number of neural elements regardless of the region of frequency. The effectiveness of a tone *or noise grows with* its frequency and duration. The greater the discrepancy in hearing *between* the ears, the greater the need for masking the better ear (*Hoc ran de Mare*). The bone conduction hearing threshold level *depends on the amount of transcranial* and pericranial transmission losses of a given test signal. Transtympanic transmission losses of *both ears* are higher than the transtemporal *ones* (*Bengt*). *Using the Rainville's* method modified by Lightfoot (*the narrow band noise vibrator placed on the forehead*) we can estimate the "cochlear reserve" *of one ear by* subtracting the *amount by* which the masking noise shifts the bone conduction *threshold*. *To* avoid the confusion between the test signal *and* a narrow *band masking noise the* pure tone must be intermittent. After defining the air conduction threshold one bone conduction receiver was placed at the *front of the* tested person more or less in its midline but inclined slightly *towards the tested ear*. *It* is easier to fasten the bone conduction vi*brator to* the forehead *where the tissues* are more homogeneous and small perceptive fluctuations *occur only*. *It* is not necessary to search for the more sensitive *points* as in the position of vibrator along the

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mastoid process whereas variations of a few mm in position cause sensitivity changes of about 10 db and it is always the possibility to set the auditory ossicles in motion so that the tone is not purely heard by bone conduction On the forehead the tactile sensations at the low frequencies are more easily discriminated from the sound Masking of the contralateral ear I have performed in the following manner An olive of the rubber tube connected with Barany s noise box was tightly fitted to the external meatus and to the mastoid process one oscillating vulcanite adapter was applied which was connected also with the noise box by means of a bifurcate metallic tube (see Fig 1) Thus the loud masking narrow band noise is transmitted by two ways to the ear i e the air conduction being unchanged in its intensity and the bone one which is calculated assuming a difference of 8 10 db as a bone conducting resistance The intensity of Barany s noise box is to be fixed at 90 db this masking can be diminished to 60 and 50 db which is sufficient in many cases of up 2000 cps to exclude the untested ear without overmasking the ear under test The normal across head difference is about 50 55 db In cases of conductive deafness the masking noise must be calculated higher at 500 cps frequency depending on degree of impairment of the bone conduction The intensity of the noise in the untested ear must not be raised to the point where it masks efficiently the bone conducted stimulus in the tested ear but this intensity must not be allowed to interfere with testing of the given ear Masking is possible if the across head difference exceeds or is at least equal to 45 db In four cases of bilateral hardness of hearing due to catarrhal changes in the middle ear in 20 25 28 and 30 year old persons I used the above method with 50 db intensity of the Barany s box enabling me to measure the real bone conduction threshold in both ears and simultaneously the difference between the two bone conduction thresholds amounting 10 22 db It is obvious that during this kind of masking one part of the noise of about 10 db is responsible for the so called across head account to the tested ear the rest however being stifled by the bones of the skull transmitting this noise This amendment must be considered when estimating the real bone conduction threshold of a given ear Then in order to eliminate this across head difference I applied the audiometric test in the interrupted form which can easily be done by lifting and dropping the decibel key At the same time the tested person is instructed not to take heed on the masking noise but on the tested tone only the intensity and gradual diminishing of which must be preserved continuously The named form of testing enabled one precise determination of bone conduction threshold to the given tone In two cases of unilateral hardness of hearing in Ménière s disease in men of 32 40 in two cases of otosclerosis in 12 and 49 year old women with loss of hearing of 32 db in the right and 56 db in the left ear and one case of unilateral deafness after labyrinthitis as well (a man of 38 with right sided loss of hearing to 72 db) the testing of bone conduction was performed in the following manner *The bone conduction receiver* was placed at front of the tested person somewhat inclined towards the

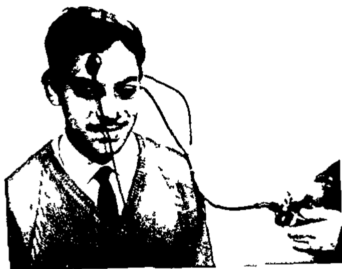


Fig 1 A 27 year old man I J with right sided protracted middle ear otitis Masking apparatus in position

tested ear In order to mask the contralateral ear it was sufficient to use the noise intensity of 50 60 and 90 db of Barany s box while the across head quantity of decibels was calculated for about 6–10 db It is evident from Fig 2 that there is a difference in behaviour of audiometric bone conducting curves by using the masking or not in two cases of hardness of hearing (a man of 32 years (Meniere s disease) and a woman of 42 (otosclerosis) with positive Carhart notch) Testing the bone conduction in two cases of congenital deafness in 14 and 16 year old boys I could state the contralateral localization of the tones C_1 C_2 transmitted through the bone oscillator placed alternately to both frontal tubera I have not found this particular phenomenon of crossed hearing perception throughout the bones of the skull in any case since Then I must mention the application of the bone conduction to the tests of Gelle Wheatstone Bing and Runge J Wever-Lawrence Smith came to the conclusion from their experiments on cats that positive or negative pressure in the middle ear has the *same effect as positive* pressure in the external ear and that the low tones are more affected than the high frequencies with a negative pressure while Bekesy stated that the named experiments convert the middle ear into a transmission system which is poorer for a strong tone than for a weak one E Arnold and P Schind[illegible] recording the calibrated variations of positive and negative air pressure in the external auditory canal have proved that diminished sensitivity for low tones in Bekesy s audiometry with positive meatal pressure is due to in creased impedance of the transmitting system The effect of Gell[illegible] on bone conduction transmitted by the Beltone A15 B C receiver [illegible] derable lessening than that with A C At 125 cps and 250 cps a [illegible]

[illegible]

mastoid process whereas variations of a few mm in position cause sensitivity changes of about 10 db and it is always the possibility to set the auditory ossicles in motion so that the tone is not purely heard by bone conduction. On the forehead *the tactile sensations at the low frequencies* are more easily discriminated from the sound. Masking of the contralateral ear I have performed *in the following* manner. An olive of the rubber tube connected *with Bárány's* noise box was tightly fitted to the external meatus and to the mastoid process one oscillating vulcanite adapter was applied which was connected also with the noise box by means of a bifurcate metallic tube (see Fig. 1). Thus the loud masking narrow band noise is transmitted by two ways to the ear, i.e. the air conduction *being unchanged in its intensity* and the bone one, which is calculated assuming a difference of 8–10 db as a *bone conducting resistance.* The intensity of *Bárány's* noise box is *to be* fixed at 90 db; this masking can be diminished to 60 and 50 db which is sufficient in many cases of up 2000 cps to exclude the untested ear without overmasking the ear under test. The normal "across head" difference is about 50–55 db. In cases of conductive deafness the masking noise must be calculated higher at 500 cps frequency depending on degree of impairment of the bone conduction. The intensity of the noise in the untested ear *must not be raised to the point where it masks efficiently the bone conducted* stimulus in the tested ear but this intensity must not be allowed to interfere with testing of the given ear. Masking is *possible if the* "across head" *difference* exceeds or is at least equal to 45 db. In four cases of bilateral hardness of hearing due to catarrhal changes in the middle ear in *20, 25, 28* and 30 year old persons I used the above method with 50 db intensity of the Bárány's box, enabling me to measure the real bone conduction threshold in both ears and simultaneously the difference between the two bone conduction thresholds amounting 10–22 db. It is obvious that during this kind of masking one part of the noise of about 10 db is responsible for the so called "across head" account to the tested ear, the rest however being stifled by the bones *of the skull transmitting this noise. This amendment must be considered* when estimating the "real" bone conduction threshold of a given ear. Then in order to eliminate this "across head" difference I applied the *audiometric* test in the interrupted form which can easily be done by lifting and dropping the decibel key. At the same time the tested person is instructed not to take heed on the masking noise but on the tested tone only, the intensity and gradual diminishing of which must be preserved continuously. *The named* form of testing enabled one precise determination of bone conduction threshold to the given tone. In two cases of unilateral hardness of hearing in Ménière's disease in men of 32, 40, in two cases of otosclerosis in 42 and 49 year old women with loss of hearing of 32 db in the right and 56 db in the left ear and one case of unilateral deafness after labyrinthitis as well (a man of 38 with right sided loss of hearing to 72 db) the testing of bone con*duction* was performed in the following manner. The bone conduction receiver was placed *at front of the tested person* somewhat inclined towards the

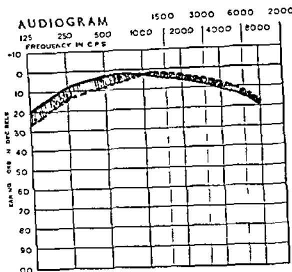


Fig 3 The Gellé's test modification as bone conduction test at overpressure of −60 mm Hg The shade lines represent changes in behaviour of the aero-tympanic and external meatus air vibrations

compressing the air in the external canal In cases of normal hearing or pure perceptive deafness the difference between the thresholds of the pure air conduction and the closed external canal will be 10–15 db for each named frequency In case of fixation of the stapes or adhesive ankylosis of the ossicular chain no difference of those thresholds can be observed at all In cases of impairments of the middle ear however the Wheatstone Bing test does agree with tests of Schwabach Rinne and Weber in a correlative pattern When the auditory canal is periodically occluded by finger the impedance of compressed air in the auditory canal adds to the vibrations of the drumhead and the ossicles transmitted simultaneously through the obturating finger from the bones surrounding the external auditory meatus giving a so called false Bing test By this the elevations and frequency of the air waves within the auditory canal become more intense and effective as a correlative pattern of the vibrating tuning fork or the bone oscillator placed to the front of the tested person Regarding the increased sensation of the bone conducting tuning fork during the test in question it must be emphasized that this event proves either normal conditions or the perceptive involvement of the tested ear On the other hand it is very helpful in discriminating between the perceptive and mixed conduction deafness but it is limited in application to cases in which the air conduction loss is 60 db or less

On testing the bone conduction after filling the external canal with a small quantity of water we get roughly one flattened curve *from the bone conducting threshold* C_2 (256) to C_4 (1000) cps whereupon *it falls a considerable number* of decibels down (see Fig 4) We consider *this evidence that a further loss* of tone perception may *follow upon relaxation of vibrating movements of*

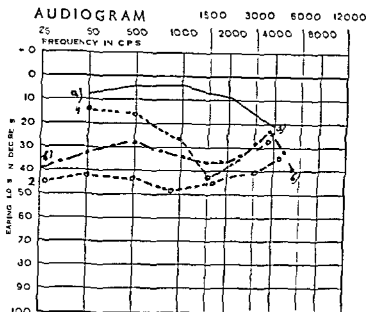


Fig. 2. *a.* A 32 year old man J. S. with right sided hardness of hearing (Ménière's disease). Broken line curve (1) after contralateral masking of 50 db Bárány's box. *b.* A 4[illegible] year old woman M. L. (otosclerosis). *Carhart notch in the right ear. The broken line curve (2) after contralateral* masking of 60 db Bárány's box.

of about 5–6 db can be noticed at 1000 cps and + 50 cm H_2O pressure this threshold shift amounts to 15 db at 4000 cps with a negative pressure of − 20 cm H_2O the threshold was 3–5 db and at a positive pressure of + 50 cm H_2O the named value *could be accounted for 1–2 db at least*. In otosclerosis the Gellé test with the calibrated air pressure gives specific audiometric findings on Békésy's audiogram showing by pressure of +60 cm H_2O a threshold loss of 0–15 db. After successful mobilization, stapedectomy or fenestration a previously negative Gellé test becomes positive of about 10–35 db (Arnold). I have seen a number of cases with normal *hearing in* whom the effect of pressure of +70–80 mm Hg in the external auditory canal (the canal opening was sealed with the oily clay around Siegle's speculum) *on the bone conduction threshold* was to lower the threshold indicating freedom of the stapes ligament. Maintenance of the threshold at the same level proves fixation of the stapes. This phenomenon is based on augmented elasticity *of the entire ossicular chain the vibration of which is tuned to higher frequency*. Drawing the curve of bone conduction threshold we get in Gellé's test one peculiar audiogram the additional story of which up to 4096 cps is formed by a vibrating air wave within the tympanic cavity and the external auditory canal (Langenbeck–Mehmke) (see Fig. 3). It must be emphasized that the strength of the pulsating tone on the *conducting apparatus of the ear is in the named* modification of Gellé's test relatively smaller than during the performance in its original form (the air Gellé). The occlusion test of Wheatstone Bing. *At each of the frequencies* gradually increasing the intensity to *250*, 500 and 1000 cps the threshold is measured with the finger on the tragus but not

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221 Old Brompton Road London S W 5,
England

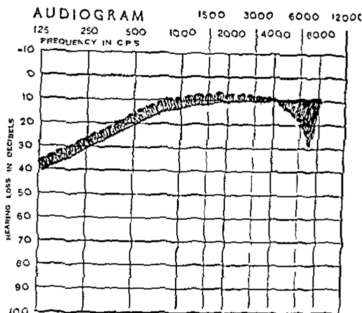


FIG 1 Runge test after filling the external meatus with water Changes in behaviour of the aerotympanic vibrations

the entire conducting apparatus overloaded by water Note that instead of air this quantity of water within the auditory canal is made to vibrate in a certain degree by a number of waves transmitted from the bones of the skull up to 1000 cps only. The named bone conducting threshold is the upper limit to which we can write down the vibrations and the phase relations of the entire conducting apparatus during performance of the Runge test

ZUSAMMENFASSUNG

Nach Bestimmung der Gehorscharfe fur Luftleitung wird ein Knochensender an die Stirn mit der Richtung zum untersuchten Ohr aufgesetzt Das Gegenohr wird *doppelartig gedampft Olivenansatz des Gummirohrchens,* welches *mit* dem Larm apparat verbunden ist, wird in den ausseren Gehorgang eingefuhrt Gleichzeitig wird der Hartgummi Knochensender, angeknupft mittels einer Gabelung mit dem Larm-*apparat, an den Warzenfortsatz aufgesetzt* Die audiometrische Knochenleitungsprüfung wird in regelmassigen Unterbrechungen durchgefuhrt, um das Überhören moglichst auszuschliessen 15 verschiedenartige Gehorstorungen sowie die Gellé-Wheatstone-Bing Runge Knochen-Versuche und gekreuzte Knochenleitungsempfindung in zwei Fallen von angeborener Taubheit werden ausfuhrlich besprochen

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AUDITORY ADAPTATION

TAUNO PALVA
Oulu Finland

From the Department of Otolaryngology University of Turku

Perstimulatory auditory adaptation for pure tones can be measured either at suprathreshold levels or at threshold The results of the former test are associated with many possible sources of error, the most important being adaptation of the control ear during median plane localization matches It is felt that this test is too cumbersome for clinical work Adaptation at threshold is easy to measure and excessive adaptation seems mostly to be associated with retrocochlear deafness Moderate adaptation values can occur in any type of perception deafness This test should belong to the routine auditory testing methods employed in clinical work

The measurement of perstimulatory adaptation has recently been included among the tests used for localization of auditory lesions However at present there is no agreement as to the values undoubtedly indicating a certain localized pathology Even in normally hearing cases the results vary widely in some of the perstimulatory tests and many contradictory views have been expressed in their clinical interpretation Nevertheless it appears obvious that when differences in the testing techniques are eliminated the differences in results will be less striking and measurement of auditory adaptation can give useful data in the evaluation of hearing impairments

My discussion today will be limited to adaptation tests with pure tones of several minutes duration The actual measurement can be made chiefly in two ways One method is to use suprathreshold tones and to measure the amount of adaptation developing in the continuously stimulated experimental ear by using the contralateral ear as a comparison ear Another method employs tones presented at threshold level in this case adaptation of the test ear can be measured as such without need to make comparison judgements with the nontested ear

Adaptation at Suprathreshold Levels

The first experiments measuring strictly perstimulatory adaptation were reported in Hood's monograph in 1950 Subsequently suprathreshold measurements have been carried out by Thwing Egan & Thwing Palva (1955) Jerger (1954) Wright (1959) and Pestalozza & Cioce (1962) The testing techniques however differed to some extent The results obtained in normal material show considerable spread the largest reported values being of the order of 35–40 db (Hood) and the lowest of the order of 5 to 10 db (Palva)

DISCUSSION

T Palva It is very timely that discussion on bone conduction has come up again this morning because we, as clinicians, have to rely in our work very much on these measurements The question on bone conduction attains even more importance when we know that in some cases there are real difficulties to perform the test in a reliable manner and in many clinics, unfortunately, the principles of the testing have not been properly worked out

First, it should be pointed out that the critical band concept of Fletcher very accurately defines the effective level of masking in the ear by white noise Some modifications make use of bands of noise in an attempt to bring the noise level down somewhat while keeping the effective level unchanged While bands of noise do have some advantages, the effective level of the band becomes smaller than its total intensity level physically precisely defined bands do not exert their influence only at the area of the band but energy spills over the adjoining frequencies and masking at center is less than expected

Secondly, increase of the interaural insulation which by using ordinary earphones we all know to be of the order of 50 db, should be seriously attempted One way to achieve this is to use insert receivers which increase the insulation by 15 to 20 db some workers have here reported figures of 40 to 50 db, but in my hands such extra insulation has never been possible to achieve But even this 15 to 20 db additional insulation gives possibilities for the examiner to avoid false results even in the worst cases viz those with bilateral conductive hearing loss

I presently favor the bone conductor to be placed on the forehead and not on the mastoid while the masking noise is led via an insert receiver into the non tested ear Recent modifications of introducing the noise via the bone conduction receiver and interrupted tones via the normal air conduction while testing the bone conduction are not convincing and one should therefore stick to the classical methods in their present improved form to guarantee correct results even in more difficult cases

A Laskiewicz Zur Bemerkung Prof Langenbecks uber den ,Interrupted working Test habe ich in meiner Arbeit diese Methode erwähnt und wegen Zeitmangel dieses Kapitel sehr kurz verfasst

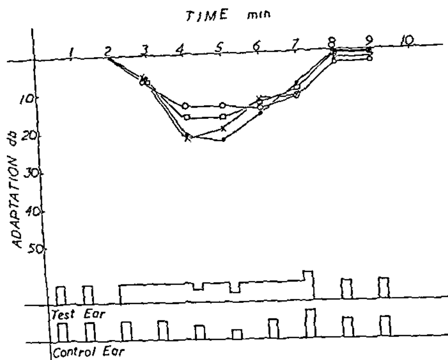


FIG 2 Results of a test run under similar conditions as in Fig 1 except that a varied intensity technique was used during the balancing matches Adaptation amounting from 13 to 23 db is demonstrated during certain periods of the test

tion matches stimuli that are more or less intense than the original adaptation stimulus While in experienced subjects the results with these two tests may vary by 5 db (Egan) in unexperienced subjects the difference may easily be of the order of 10 to 15 db It is also noteworthy that a short temporary increase of intensity during the balancing match tends to decrease the adaptation from the level obtained either during the original intensity or a weaker tone match

The suprathreshold test in this form has even more serious limitations however All the investigators mentioned above used a comparison stimulus of 10 to 20 sec duration (generally 15 sec) assuming that no appreciable adaptation would occur in the control ear But it was pointed out by Wright (1960) that this assumption *is not valid* and this fact indeed is crucial to the test If adaptation develops in the control ear rapidly, then the measured value of perstimulatory adaptation is small *and vice versa*

Wright (1960) was able to prove this point quite conclusively by two different methods The experimental ear was first fully adapted *during a 7 min* stimulation and midplane localization judgements were thereafter *obtained* by stimulating the control ear with only 1 sec long tones Adaptation of the order of 50 db was measured by this means at 90 db sensation level which … than by the conventional method with fixed *intensity*

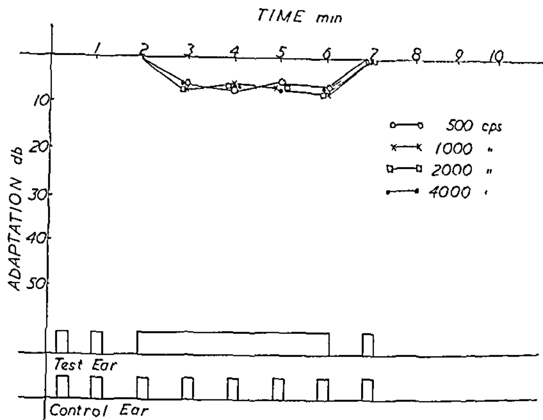


Fig. 1. Average results of a test run for perstimulatory fatigue at 80 db SL for two ears of experienced listeners. Using a fixed intensity technique adaptation of the order of 6 to 7 db is maintained through the whole test run, the balancing match was made during a 15 sec test period.

at 60–80 db hearing level. The results of the others show better conformity, the amount of perstimulatory adaptation after 3 min stimulation being generally of the order of 20 to 25 db.

From these data one readily assumes that there must be serious differences either in the testing technique or in the development of perstimulatory adaptation as such in normal ears. Consequently, before suprathreshold tests can be applied *in the clinic the reasons for the discrepancies should be clarified.*

In the suprathreshold tests, loudness balances in their proper sense cannot be made but they must be substituted with a judgement of median plane localization, a phantom sound appearing somewhere within the observer's head. This in itself can make the test more difficult. In some sophisticated listeners the spread of results from the median plane judgement would not be more than a few decibels (Wright, 1960) but in unsophisticated subjects the area of uncertainty, especially for the low tones, is quite often of the order of 10 to 20 db.

Egan has pointed out another shortcoming of the test, viz. the development of an absolute loudness standard for the comparison stimulus if a fixed intensity method is used. The amount of adaptation tends to be underestimated *as compared with a method of varied intensity in which the absolute* loudness standard is broken by presenting to the subject, during the localiza-

unrealistic and cannot be used as normal reference values If suprathreshold adaptation tests are used the experimental ear must first be fully adapted and midplane localization judgements should then be obtained with only 1 1 5 sec long stimuli in the control ear Application of suprathreshold adap tation tests in clinical routine does not seem to be promising because it is doubtful whether the results obtained would be worth the trouble involved in the time consuming measurement

Adaptation at Threshold Levels

The use of the tone decay test or excessive threshold adaptation, goes back to the 19th century Gradenigo in 1893 reported that in acoustic tumors the patients responded to a maximally vibrating tuning fork only a few seconds the initially loud tone disappearing quickly This very astute observation fell into oblivion for many decades and not until 1944 did Schubert suggest that this method be included in audiometric tests The patient was allowed to listen to a 5 db sensation level tone until the tone disappeared the intensity was thereafter raised in 5 db steps until a plateau was reached or the maximum limit of the audiometer did not permit following the receding tone Schubert concluded that adaptation is limited to end organ lesions and increases with frequency as well as with advancing age Adaptation values of the order of 18 to 25 db were obtained in these ears

cases however the opinions as to which types of deafness show this phenomenon diverge widely it has been claimed to be solely an indication of end organ deafness of nerve deafness of both end organ and nerve deafness or to appear only in central deafness

It seems first appropriate to examine more closely the measuring techniques because due to different methods the results may not be directly comparable with each other In addition to the technique of Schubert which has also been used by Hood (1955) Carhart (1957) Sorensen (1962) and Parker *et al* (1962) another technique involving the use of an automatic Bekesy type audiometer has been extensively *applied* By the latter method the patient himself makes a continuous *recording* of the development of adapta tion as a function of time generally for a 3 to 5 min period During this type of test the tone successively increases to 100 % audibility and decreases to 0 % audibility whereas *in* the *original* technique the intensity of the test tone is constant during any time that the patient reports hearing the tone One would therefore assume that adaptation as measured by the automatic technique would be less than as measured by the fixed intensity technique, and indeed this seems to be the case

Thus Hood for instance reports that adaptation of the order of 20 to 30 db is a phenomenon characteristic of end organ deafness and can in this respect be used as a diagnostic criterion On the other hand Palva s (1957 1961) results in 154 ears recorded with automatic audiometer show

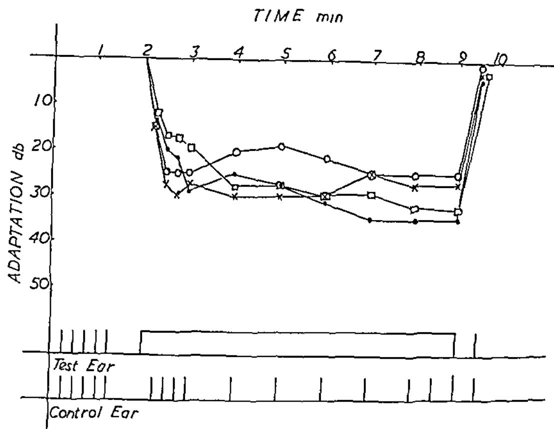


FIG 3 Results of a test run under similar conditions as in Fig 1 except that the balancing matches were made more frequently with only 1 sec long comparison tones It should be noted that adaptation develops very rapidly and only minor changes are seen after one minute of the test The curves strongly support the view that adaptation of the control ear during the 15 sec balancing matches leads to unrealistically small values of adaptation recorded from the test ear

Wright used also another method to test the development of adaptation in the control ear after full adaptation of the experimental ear the time taken by the phantom sound to move from the control ear into midplane was measured This time proved to be the shorter the lower the initial starting level in the control ear and the lower the adaptation intensity in the experimental ear It was also noted that the phantom sound appeared at midline for a wide range of intensities especially at the lower tones—a fact already referred to above

*Another factor suggesting limitations to the use of suprathreshold measure*ments is the great variability of individual listeners At 60 to 80 db sensation levels the standard deviations at least in the studies of Palva and Jerger were of the order of 6 to 12 db This finding apparently is at least partly due to the different rates of adaptation in the control ear and partly due to individual differences as such

It is evident from the foregoing that the wide range of adaptation values reported in normal ears depend upon many factors the most influential being the unaccounted for adaptation of the comparison ear Therefore the use of comparison stimuli of 10 to 20 sec duration yields results that are

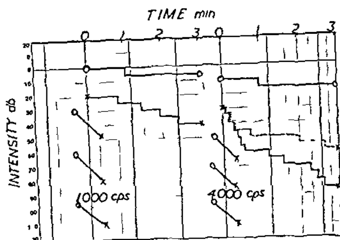


Fig 5 A patient with tinnitus in the left ear associated with a 20 to 30 db hearing loss and episodes of slight vertigo Left corneal reflex was sluggish but no other evidence favoring cerebellopontine angle tumor was found Recruitment tests showed no recruitment adaptation in the right ear was normal At 4000 cps in the left ear a 55 db adaptation loss was recorded several times (continuous line) while on some later occasions only 30 db loss (broken line) was demonstrated Lesion of the nerve is still strongly suspected

tion (20 to 30 db) This view especially as regards the eighth nerve has been favored by Reger & Kos (1952) by Lierle and Reger, and by Kos (1955) and later by Jerger *et al* (1958) Yantis (1959) Sorensen & Parker *et al* (1962) etc Generally, but not always the threshold loss in these cases was excessive Thus one verified acoustic neurinoma among Sorensen's eight cases showed adaptation of 30 db during 3 min stimulation one of Palva's neurinoma cases 25 db and apparently the three tumor cases in Pestalozza and Cioce's series behaved much in the same fashion

If auditory adaptation is a phenomenon associated with end organ or acoustic nerve lesions it should be possible to demonstrate it in the electro physiological tests A search of the literature indeed reveals that there is some evidence in favor of this Gisselsson & Sorensen (1959) working with guinea pigs and Mantegazzini *et al* Kiang & Peake (1960) and Ruben *et al* (1962) with cats, deny the existence of adaptation in the cochlear potentials while Shimizu *et al* (1957) in guinea pigs report some reduction after stimulation at 70 90 db levels for 20 to 30 min In action potentials Sorensen (1959) observed decrease in response to clicks when the nerve was simultaneously stimulated with white noise and Hernandez Peon *et al* demonstrated marked adaptation in the electrical potentials recorded from the more central pathways viz the dorsal cochlear nucleus

Clinical evidence presented hitherto clearly shows that even excessive adaptation sometimes occurs in normally hearing ears (Carhart 1957 Hinchliffe 1959 Palva & Palva 1962) seldom in cases with typical end-organ disease and fairly frequently in lesions either of the cochlear nerve or more

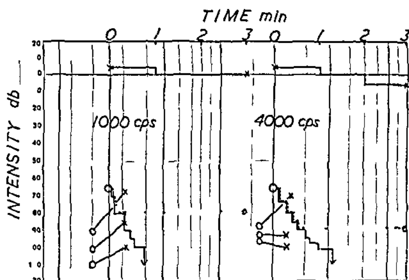


FIG. 4. A patient with multiple cysts and polyps in the right maxillary antrum with a sense of fullness in the right ear combined with a flat 60 db sensorineural hearing loss. Recruitment tests showed partial recruitment at 1000 cps and overrecruitment at 4000 cps. Tone decay tests in the right ear indicated large perstimulatory loss at repeated tests prior to operation (continuous recording). One month postoperatively sensation of fullness in the ear had disappeared while deafness persisted. Adaptation tests (broken lines) now showed repeatedly only 15 to 25 db loss.

that adaptation exceeding 10 db appears in only 13 % of cases of recruiting perceptive deafness.

Contradictory results with similar techniques have also been reported. Sorensen (1962) using essentially the method of Schubert and of Hood noted in 114 cases of recruiting deafness adaptation of less than 10 db in 54 cases, more than 10 db but reaching a plateau in 58 cases, and in only 2 cases did pronounced tone decay appear. On the other hand, in non-recruiting deafness the corresponding figures in 42 cases were 5, 2 and 35 respectively. Thus in end organ disease an excessive adaptation was exceptional rather than the rule.

Obviously the original technique of presenting a continuous tone to the test ear as contrasted with automatic recording is to be favored if maximal figures for adaptation at threshold are desired. However, it has been shown that also automatic recording can disclose excessive threshold losses, and its usefulness is increased by the possibility of making successive audiograms with interrupted and continuous test tones. In easily adapting cases the discrepancy between these two tests has been found to be considerable, although also in this respect contradictory reports have appeared (Hood 1955, Jerger 1960, Parker *et al.*, Harbert & Young 1962, etc.). Either technique can therefore be used but direct comparison of results is only possible if identical techniques have been employed.

The recent trend in threshold tone decay testing is to link excessive adaptation to acoustic nerve or central pathways while end organ disease would show, as a rule, either normal adaptation (less than 10 db) or some adapta-

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Dept of Otolaryngology University of Oulu
Finland

DISCUSSION

H Langenbeck Wir können einmal die Adaptation, dann auch *die Erholung nach der Ermüdung* oder Adaptation messen Das erste ist die Schwellen Schwundtestung nach Schubert Carhart *Die Erholung oder Readaptation* messen wir durch Bestimmung *der* Tonschwellen in einem periodisch fur 70 millisec unterbrochenen Gerausch Die Besserung *der Schwellen im* unterbrochenen Gerausch gegenuber der Messung im Dauergerausch zeigt *wie stark sich* das Gehor in der kurzen Gerauschpause von 70 millisec erholt hat *Wir haben damit ein Mass für* die Geschwindigkeit der Readaptation und können *in einem kurzen Test* fur den ganzen Tonbereich feststellen wie sich die Readapt*ation in den verschiedenen* Tonlagen verhalt Diese Messmethode stellt eine Fortentwicklung von Versuchen Boccas dar und steht mit der Schwellenschwundtestung gut im Einklang

F Pecca Dr Palva pointed out most rightly how difficult it is to employ adaptation tests based on binaural balance *in clinical routine* due to adaptation phenomena taking place in the *contralateral ear* and to interaural interference or cross action [illegible] should like to remind in complete *agreement with Mr* Langenbeck, that the

centrally Moderate adaptation during 3 min stimulation, of the order of 10 to 30 db, may occur in any type of perception deafness and allows no diagnostic criteria to be made

Even if the trend for excessive threshold adaptation seems clearly to point more to lesions of the nerve than to end organ lesions one should not be too categorical in conceding the tone decay test a pathognomonic role in the localization of the lesions evidence obtained from other tests both audiological and clinical, should accord with the findings before a definite diagnosis is made

ZUSAMMENFASSUNG

Die perstimulatorische Gehöradaptation kann entweder mit überschwelligen oder schwellenwertigen Tonen gemessen werden Die Resultate mit überschwelligen Tönen sind mit vielen Fehlerquellen verknupft die wichtigste sei die Adaptation des Kontrollohres während der Tonbalancierung Diese Probe scheint zu lästig für die klinische Routinearbeit zu sein Mit schwellenwertigen Tonen dagegen ist die Adaptation leicht zu messen, ubermässig grosse Adaptationswerte erscheinen meistens in Fällen von retrocochlearer Taubheit Werte von 10 bis 30 db sind in allen Gruppen von perzeptiver Schwerhorigkeit zu finden Adaptationsproben mit schwellenwertigen Tonen sollten in die Routineproben gehoren

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Dept of Otolaryngology University of Oulu, Finland

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I should like to remind, in complete agreement with Mr Langenbeck, that the

interrupted noise test, or recovery time test, at which we worked independently at about the same time, with irrelevant technical differences, proves to be one of the most precious monaural clinical test for assessing disorders of function located at the level of the cochlear receptors The test is very precise, very little time-consuming and it is not subject to that sort of interference which often invalidates other adaptation tests The test has not become very popular so far, but I think that it deserves to become more widely known and used in clinical audiological practice

T Palva (Reply) First I should like to thank my discussers for their remarks concerning measurement of auditory adaptation in interrupted noise At the present time I too, am working with one modification of noise audiometry in adaptation tests However, I should like to point out that my discussion this morning had to do only with adaptation for pure tones of several minutes duration and the discussion of noise tests in this connection is somewhat off the point I have specially wanted to take up this issue with pure tones because here it is very easy to appreciate the profound effect of testing techniques on the results Only when the techniques become standardized agreed upon, and applied strictly in similar manner can we hope for results that are generally acceptable as criteria for classification of hearing losses from the audiological viewpoint

NETZHAUTARTERIENDRUCK-VERÄNDERUNGEN NACH LÄRMBELASTUNG

G. VASSOULIS und K. A. KONSTAS
Thessaloniki, Griechenland

Bei 28 ohrgesunden Versuchspersonen wurde der Netzhautarteriendruck unter Lärmbelastung laufend kontrolliert. In der Mehrzahl der Fälle konnte dabei eine Blutdruckerniedrigung festgestellt werden, die in der Hälfte nahezu aller Fälle als signifikant anzusehen wäre. Diese Blutdrucksenkung war in der fünften Minute nach Beginn der Lärmeinwirkung feststellbar. Der gleichzeitig gemessene Brachialisdruck erwies sich dabei als nahezu unverändert. Die Blutdruckerniedrigung an der Zentralarterie der Netzhaut wird als Folge einer Vasodilatation im Carotiskreislaufgebiet angesehen. Da es, wie bekannt, unter Lärmeinwirkung im Hautkreislauf zu einer Vasokonstriktion kommt, wird angenommen, dass beide im Grunde verschiedene Kreislaufreaktionen Teilausdrucke ein und derselben reflektorischen Reaktion des Vasomotorenzentrums infolge der Lärmeinwirkung darstellen.

Durch Versuche bei Erwachsenen (Lehmann 1957, Lehmann & Tamm 1958) und bei Kindern (Matthias & Jansen 1962, Jansen & Rey 1962) konnte ermittelt werden, dass unter Lärmbelastung gewisse Kreislaufreaktionen recht regelmässig zu beobachten sind. So konnte unter Verwendung der kreislaufanalytischen Methode nach Wetzler-Boger (Lehmann & Tamm 1958) während der Lärmeinwirkung eine deutliche Verminderung des Herzschlagvolumens sowie eine Vermehrung des peripheren Widerstandes nachgewiesen werden. Währenddessen blieben Pulsfrequenz und Blutdruck (Abb. 1) nahezu unverändert. Untersuchungen andererseits der Fingerdruckamplitude nach der Methode von Brecht und Boucke (Jansen 1962, Matthias & Jansen 1962) und der Hautdurchblutung durch die Methode der Hautdurchleuchtung nach Mathes (Matthias & Jansen 1962) unter Lärmbelastung ergaben eine signifikante Verminderung des Blutabflusses im Kapillargebiet des Fingers und des Ohrläppchens als Folge einer Verengung der präkapillaren Arteriolen. Diese Kreislaufreaktionen, die völlig unabhängig von der psychischen Wirkung des Lärmes sind, werden als vegetative Reaktionen des Kreislaufsystems aufgefasst.

Obenerwähnte Ergebnisse der experimentellen Lärmforschung beziehen sich hauptsächlich auf einen Teil des gesamten Kreislaufs, nämlich auf die Hautzirkulation.

Wir haben uns zur Aufgabe gestellt, eventuelle Auswirkungen der Lärmeinwirkung bei einem anderen Kreislaufgebiet zu erforschen, indem wir bei 28 ohrgesunden Versuchspersonen den Netzhautarteriendruck während einer Lärmbelastung von 90 db, 1000 Hz durch laufende Messungen kon-

interrupted noise test, or recovery time test, at which we worked independently at about the same time, *with irrelevant technical differences, proves to be one of* the most precious monaural clinical test for assessing disorders of function located at the level of the cochlear receptors. The test is very precise, very little time consuming and it is not subject to that sort of interference which often invalidates other adaptation tests. The test has not become very popular so far, but I think that it deserves to become more widely known and used in clinical audiological practice.

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TABELLE 1

Fall Nr	Alter	Geschlecht	Ausgangswert	Nach Lärmbelastung 2	Nach Lärmbelastung 5
1	54	♂	11/7 20/30	11/6 28/40	10/6 22/32
2	52	♂	10/6 30/48	11/6 32/50	11/6 22/30
3	50	♂	13/8 38/70	13/8 40/80	13/8 28/42
4	20	♀	10/7 22/32	10/6 22/40	10/6 20/30
5	68	♂	17/8 40/100	17/9 40/85	17/9 30/60
6	33	♂	9/6 24/40	9/6 24/40	9/6 24/40
7	52	♂	11 5/8 30/60	11/7 30/60	10/7 24/50
8	20	♀	11/7 30/55	12/8 30/60	13/8 30/52
9	55	♀	11,5/8 26/50	11,5/8 26/50	11 5/8 22/46
10	65	♂	13/7 34/70	14/9 40/70	14,5/10 32/58
11	26	♂	11/7 30/52	11 5/7 38/50	11 5/7 25/42
12	29	♂	11/7 30/49	10/7 5 32/52	10/7 30/46
13	25	♂	13/9 40/60	13/9 32/52	13/9 30/52
14	27	♂	16/8 32/70	16/8 32/70	16/8 30/60
15	34	♂	12/8 32/46	12/8 36/52	12/8 30/42
16	18	♂	10/7 30/50	10/7 30/40	10/7 22/36
17	30	♀	10/7 28/40	10/7 30/42	10/7 26/34
18	30	♀	11,5/7 30/52	11,5/7 32/52	11 5/7 24/36
19	16	♀	10/7 28/42	10/7 28/42	10/7 26/40
20	66	♂	13/8 40/60	13/8 40/60	13/7 32/50
21	25	♂	12/6 32/48	12/6 34/52	12/6 28/42
22	22	♂	11/7 30/42	14/7 30/42	11/7 28/40
23	69	♂	13/7 32/44	12/7 34/50	12/7 26/32
24	40	♀	16/9 50/100	16/9 55/100	16/9 28/70
25	22	♀	11/6 35/72	11/6 35/72	11,5/6 5 30/52
26	17	[illegible]	13/8 30/50	13 5/8 34/55	14/8 20/35
27	14	♂	12/6 5 26/42	12/6 5 28/44	12/6,5 22/40
28	49	♂	11 5/7 30/80	11 5/7 32/80	11/71 30/80

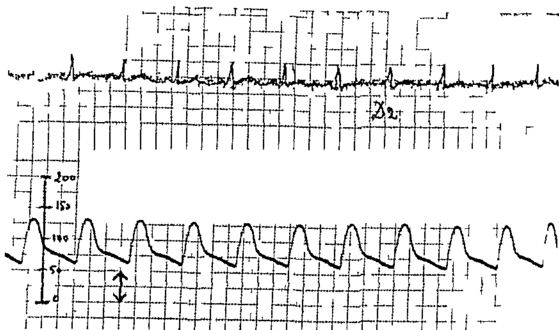


Abb. 1. E[illegible] arterieller Blutdruck der Femoralis. Beginn (↕) Lärm [illegible] Wirkung keine Veränderung [illegible]

trollierten. Wie bekannt (Weigelin) entspricht der bei der Ophthalmodynamometrie optisch abgelesene Blutdruck der Arteriae centralis retinae dem jenigen der Arteriae ophthalmicae, die den ersten intrakraniellen Ast der Carotis interna darstellt. Unter der Voraussetzung, dass Augenbinnendruck, Hirndruck und Brachialisdruck konstant bleiben, deuten Netzhautarteriendruck-Schwankungen auf ähnliche Schwankungen des Carotisdrucks hin.

Versuchsanordnung. Bei jeder Versuchsperson wurde zuerst Brachialis- und Netzhautarteriendruck festgestellt. Ersterer durch einen Riva-Rocci-Manometer, letzterer durch einen Baillartschen Ophthalmodynamometer nach vorheriger medikamentöser Erweiterung der Pupille und lokalen Anästhesie der Bindehaut. Es folgte eine Pause von 10 Minuten, wobei jede Versuchsperson auf einem Liegestuhl ruhig sass und anschliessend wurden Brachialis- und Netzhautarteriendruck nochmals gemessen. Der somit ermittelte Ruhewert wurde als Ausgangswert bewertet.

Nun wurde jede der 28 Versuchspersonen einer 5 Minuten langen Lärmbelastung von 90 db 1000 Hz mittels des japanischen Trio AG 8 Apparates unterstellt. Am Ende der zweiten Minute wurden Brachialis- und Netzhautarteriendruck wieder gemessen. Eine dritte Messung an beiden Messstellen erfolgte kurz vor Beendigung der Lärmbelastung, d. h. am Ende der fünften Minute vom Beginn der Lärmeinwirkung an. Bei einer Anzahl von Versuchspersonen, nämlich bei denjenigen, bei denen eine signifikante Netzhautarteriendruck-Veränderung festgestellt wurde, folgte eine vierte Messung 10 Minuten nach Aussetzen der Lärmeinwirkung.

Die Messergebnisse sind tabellarisch zusammengestellt (Tabelle 1). In der ersten Rubrik sind die Ausgangswerte, in der zweiten und dritten die während der Lärmbelastung ermittelten Werte aufgezeichnet. Brachialis-

TABELLE 2

Fall Nr	Alter	Geschlecht	Ausgangswert	Nach Lärmbelastung 2	5
			12/7	12/7	12/7
1	20	♂	25/52	22/40	24/44
			10/6	11/7	11/7
2	13	♀	24/40	22/32	22/32
			11/7	12/9	12/9
3	12	♂	24/48	28/48	28/48
			10/6	11/6	11/7
4	12	♂	32/46	28/40	24/40
			12 5/8	12/8	12/8
5	16	♂	30/52	30/50	30/52
			11/7	10/7	10/7
6	18	♀	30/50	30/50	22/38
			10,5/7	11 5/7	11 5/7
7	14	♂	30/50	30/50	30/50
			11 5/7	11/7	11/7
8	15	♀	28/49	30/46	30/42
			11/7	11/7	11/6
9	9	♀	24/40	24/40	26/40
			10 5/7	10 5/7	10 5/7
10	9	♂	30/44	30/44	30/44
			12/7	12/7	12/7
11	13	♂	28/42	24/42	24/42

dem Vergleich der Ausgangswerte mit denen der dritten Messung entnommen worden. Denn bei der zweiten Messung, d. h. zwei Minuten nach Beginn der Lärmbelastung, erwies sich im allgemeinen der Netzhautarteriendruck entweder gleich (Fälle Nr. 6, 7, 9, 16, 19, 20, 22, 25 und 28) oder meistens etwas höher als der entsprechende Ausgangswert (Fälle Nr. 1, 2, 3, 4, 8, 10, 15, 17, 18, 21, 23, 24, 26 und 27). Nur in drei Fällen (Fälle Nr. 5, 13 und 16) konnte eine geringe Blutdruckverminderung nachgewiesen werden.

Bei den 12 Fällen, bei welchen eine signifikante Netzhautarterienblutdruckverminderung unter Lärmbelastung beobachtet wurde, ist eine vierte Messung an beiden Messstellen 10 Minuten nach Beendigung der Lärmeinwirkung unternommen worden. In fünf Fällen erreichte der Netzhautarteriendruck den Ausgangswert wieder (siehe Abb. 2), während bei den übrigen sieben Fällen derselbe höher als bei der dritten Messung, jedoch deutlich unter dem Ausgangswert zurückblieb. Wir führen hierzu ein Beispiel aus dem Falle Nr. 3 an: Ausgangswert 38/70. Nach zwei Minuten Lärmbelastung 40/80, am Ende der fünften Minute 28/42. Zehn Minuten nach Lärmbeendingung 32/52. Brachialisdruck an allen Messungen 13/8.

Im ganzen genommen verhält sich der mittlere Ausgangswert des distolischen Netzhautarteriendruckes zu demjenigen am Ende der Lärmbelastung wie 31,1 : 24,4 g. Die gleichen mittleren Werte des systolischen Druckes ver-

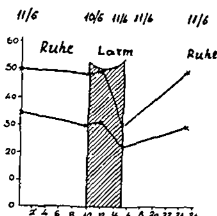


Abb. 2

druckwerte sind in cm³ Hg, Netzhautarteriendruckwerte in Gramm angegeben. Eine Umrechnung der letzteren in mm³ Hg, die eine Bestimmung des Augenbinnendruckes mittels Tonometers erfordern würde, wurde nicht als notwendig angesehen, denn es handelte sich ja nicht um die Bestimmung absoluter Werte, sondern um die Erfassung eventueller Veränderungen.

Aus der Tabelle 1 ist zu ersehen, dass der Brachialisdruck während der Lärmbelastung nahezu keine nennenswerten Veränderungen aufwies. Bei der Mehrzahl der Fälle (17mal) blieb er unverändert, oder so gut wie unverändert (3mal Unterschiede von 0,5 cm³ Hg). Sechsmal wurde eine Senkung des systolischen bzw. des diastolischen Brachialisdruckes festgestellt, die jedoch nicht 1, seltener 1,5 cm³ Hg übertraf (Fälle Nr. 1, 4, 7, 12, 20, 23). Fünfmal wurde eine meistens geringe Blutdruckerhöhung nachgewiesen (Fälle Nr. 2, 5, 8, 10, 26). Im ganzen genommen verhält sich der mittlere Wert des diastolischen Brachialisdruckes vor und am Ende der Lärmeinwirkung wie 7,2 : 7,3, derjenige des systolischen Brachialisdruckes wie 11,9 : 12.

Im Gegensatz dazu liessen sich bei unseren Versuchspersonen oft signifikante Schwankungen des Netzhautarteriendruckes, und zwar im Sinne einer Blutdruckerniedrigung, die 10 g und mehr betrug, feststellen. Dies traf in 12 Fällen zu (Fälle Nr. 2, 3, 5, 10, 13, 16, 18, 20, 23, 24, 25 und 26), d. h. nahezu die Hälfte der untersuchten Versuchspersonen. Dabei erwies sich der Brachialisdruck entweder unverändert (Fälle Nr. 13, 16, 18, 24, 25) oder gar erhöht (Fälle Nr. 2, 5, 10, 26). Nur bei drei Fällen (Fälle Nr. 2, 5, 10, 26) war der Brachialisdruck niedriger gefunden.

In 10 Fällen fand sich der Netzhautarteriendruck während der Lärmbelastung kaum oder nicht verändert (Fälle Nr. 1, 4, 6, 8, 12, 15, 19, 22, 27 und 28), während in den übrigen 6 Fällen eine merkbare, jedoch nicht signifikante Blutdruckverminderung (Fälle Nr. 7, 11, 14, 17, 21 und 23) festgestellt werden konnte.

Die Netzhautarteriendruck-Verminderung ist bei der dritten Messung, d. h. am Ende der fünften Minute nach Beginn der Lärmeinwirkung, festgestellt worden. Obengenannte Wertunterschiede in beiden Messstellen sind aus

TABELLE 2

Fall Nr.	Alter	Geschlecht	Ausgangswert	Nach Lärmbelastung 2′	5′
			12/7	12/7	12/7
1	20	♂	25/52	22/40	24/44
			10/6	11/7	11/7
2	13	♀	24/40	22/32	22/32
			11/7	12/9	12/9
3	12	♂	24/48	28/48	28/48
			10/6	11/6	11/7
4	12	♂	32/46	28/40	24/40
			12,5/8	12/8	12/8
5	16	♂	30/52	30/50	30/52
			11/7	10/7	10/7
6	18	♀	30/50	30/50	22/38
			10,5/7	11,5/7	11,5/7
7	14	♂	30/50	30/50	30/50
			11,5/7	11/7	11/7
8	15	♀	28/49	30/46	30/42
			11/7	11/7	11/6
9	9	♀	24/40	24/40	26/40
			10,5/7	10,5/7	10,5/7
10	9	♂	30/44	30/44	30/44
			12/7	12/7	12/7
11	13	♂	28/42	24/42	24/42

dem Vergleich der Ausgangswerte mit denen der dritten Messung entnommen worden. Denn bei der zweiten Messung, d. h. zwei Minuten nach Beginn der Lärmbelastung, erwies sich im allgemeinen der Netzhautarteriendruck entweder gleich (Fälle Nr. 6, 7, 9, 16, 19, 20, 22, 25 und 28) oder meistens etwas höher als der entsprechende Ausgangswert (Fälle Nr. 1, 2, 3, 4, 8, 10, 15, 17, 18, 21, 23, 24, 26 und 27). Nur in drei Fällen (Fälle Nr. 5, 13 und 16) konnte eine geringe Blutdruckverminderung nachgewiesen werden.

Bei den 12 Fällen, bei welchen eine signifikante Netzhautarterienblutdruckverminderung unter Lärmbelastung beobachtet wurde, ist eine vierte Messung an beiden Messtellen 10 Minuten nach Beendigung der Lärmeinwirkung unternommen worden. In fünf Fällen erreichte der Netzhautarteriendruck den Ausgangswert wieder (siehe Abb. 2), während bei den übrigen sieben Fällen derselbe höher als bei der dritten Messung, jedoch deutlich unter dem Ausgangswert zurückblieb. Wir führen hierzu ein Beispiel aus dem Falle Nr. 3 an. Ausgangswert 38/70. Nach zwei Minuten Lärmbelastung 40/80, am Ende der fünften Minute 28/42. Zehn Minuten nach Lärmbeendigung 32/52. Brachialisdruck an allen Messungen 13/8.

Im ganzen genommen verhält sich der mittlere Ausgangswert des diastolischen Netzhautarteriendruckes zu demjenigen am Ende der Lärmbelastung wie 31,1:24,4 g. Die gleichen mittleren Werte des systolischen Druckes ver-

halten sich wie 55 : 45 g. Ähnliche Blutdruckmessungen sind zum Vergleich bei einer Gruppe von tauben Versuchspersonen im Gange. Bis jetzt sind elf solche Personen untersucht worden. Wie aus der Tabelle 2 zu ersehen ist, ist nur einmal (Fall Nr. 6) eine signifikante Blutdruckerniedrigung an der Arteria centralis retinae zu verzeichnen. Bei den übrigen Fällen bleibt der Netzhautarteriendruck entweder unbeeinträchtigt oder zeigt eine unbedeutende Erniedrigung.

Der *mittlere* Wert des diastolischen Netzhautarteriendruckes vor und nach Lärmbelastung verhält sich wie 27,7 : 26, derjenige des systolischen Druckes wie 46,6 : 43. Wir *beabsichtigen zu diesem Thema nochmals nach* Abschluss der Messungen an dieser Kontrollgruppe Stellung zu nehmen. Inzwischen sind Untersuchungen *über den etwaigen Einfluss der Ultra*schallwirkung auf den Netzhautarteriendruck ebenfalls im Gange.

DISKUSSION

In der Mehrzahl der untersuchten Versuchspersonen lässt sich nach fünf Minuten Lärmbelastung eine Netzhautarteriendruck-Verminderung feststellen, die in der Hälfte nahezu aller Fälle als signifikant anzusehen ist. Dabei bleibt der Brachialisdruck unverändert oder nahezu unverändert, so dass man von einer diskordanten Blutdrucksenkung am Ophthalmica-Kreislaufgebiet sprechen kann. Da Hirndruck und Augenbinnendruck als konstant angenommen werden können, weist diese Blutdruckerniedrigung auf eine ähnliche Blutdruckerniedrigung im Carotiskreislaufgebiet hin. Diese kann entweder auf eine Verengung des zuführenden Astes oder eher auf eine Erweiterung der präkapillaren Arteriolen im Gehirn zurückgeführt werden. Während also unter Lärmbelastung, wie schon bei der *Einleitung* erwähnt wurde, im Hautkreislaufgebiet eine Vasokonstriktion auftritt, scheint *es im Hirnkreislauf dagegen zu einer Vasodilatation zu kommen.* Letztere tritt im Vergleich zur Vasokonstriktion der Haut, die innerhalb der ersten Minute nach Lärmeinwirkung zu verzeichnen ist (Jansen), später auf. Es ist anzunehmen, dass diese verschiedenen Kreislaufreaktionen Teilausdrucke ein und derselben, durch die Lärmeinwirkung bedingte reflektorische Reaktion des Vasomotorenzentrums darstellen. Wahrscheinlich tritt eine Vasodilatation während der Lärmbelastung auch an anderen Kreislaufgebieten (Nieren, Herz z. B.) auf. So wäre es zu erklären, dass trotz Vermehrung des Strömungswiderstandes im Hautgebiet während der Lärmbelastung der Brachialisdruck unverändert oder so gut wie unverändert zu bleiben pflegt.

SUMMARY

While deaf people do not show any *rise or change in general as regards the blood* pressure in their central retinal artery, the majority of healthy individuals shows a notable rise a few minutes after the production of noise. The brachial or the intra-arterial femoral pressure does not show noticeable variations.

RÉSUMÉ

Les sourds ne montrent pas de variation en ce qui concerne la pression artérielle (artère de la rétine centrale) D'autre part la plupart des individus sains presentent une augmentation importante et cela surtout quelques minutes apres le commencement du bruit La pression de l'artère brachiale et la pression intra artérielle de l artère femorale ne présentent pas de variations considérables

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Dor Konstas Universitäts Augenklinik
Thessaloniki, Griechenland

DISCUSSION

G de Wit We too used the ophthalmodynamometer of Baillard After stimulation of the vestibular apparatus by means of the parallel swing we found, after a lowering, that the retinal arterial pressure raised above the initial value in some persons Is there a parallel with your investigations of the cochlear function?

G Yannoulis (Antwort) zu de Wit Erst nach den ersten 5 Minuten wurde eine Senkung beobachtet, wie es durch die Projektion und den Text zu ersehen ist

SUPER- AND SUBLIMINAL BINAURAL BEATS

J. J. GROEN
Utrecht, The Netherlands

From the Department of Otolaryngology (Head: Prof. Dr. P. G. Gerlings)
Utrecht State University

Based upon the work of Lane (1925) and Lehnhardt (1961) the phenomenon of binaural beats was further studied. The behaviour of the beats as a function of frequency points to three distinctly different frequency regions with an optimum audibility in the range from 90 to 800 cps, less clear from 850 to 1100 cps, audibility falling rapidly beyond 1100 to 1400 cps, disappearance at 1500 cps. In the optimum range the loudness modulation of binaural beats is comparable to that of a monaural about 2 db modulated tone. Binaural beats are detectable at levels of 20 db below threshold in one ear, if the level in the other ear is above or near threshold.

INTRODUCTION

Binaural beats are an interesting phenomenon, especially those which occur at near threshold levels. These beats, apparently resulting from an interference between volleys from both ears, have been discussed by Lane (1925), Matzker (1958), Lehnhardt (1961) and others. The possible underlying neural mechanism is supposed to be located in the superior olives, in each of which both cochleae are represented (Fig. 1). Volleys from the two auditory pathways converge on the olive. The summation of their activities passes from maximum when the volleys are synchronous to a minimum when they are exactly out of step. Then the volleys of one ear arrive just between those of the other ear. The stimulation in the synapses of the superior olive thus fluctuates periodically, giving rise to an amplitude modulated tone. Typical aspects of binaural beats are the following:

(*a*) They are produced in a restricted frequency band with an optimum audibility between 90 and 800 cps, beyond which frequency detectability rapidly declines.

(*b*) In the intensity range a curious behaviour can be observed (Lehnhardt 1961): if a pure tone is presented above threshold in one ear and the other in the *contralateral ear at a subliminal threshold level, beats can still* be heard.

The upper frequency limit for the appearance of binaural beats has been one of the parameters investigated by us. The other quantity studied has been the apparent loudness modulation of the binaural beat at different loudness levels. The results are reported in the following paragraphs.

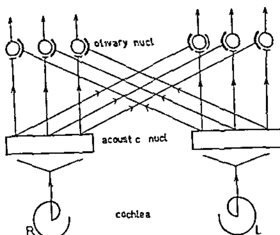


Fig. 1. Schematic drawing of auditory pathways from cochlea to superior olive. Both cochleae are represented in each olive.

Audibility of Binaural Beats as a Function of Frequency

If one ear listens to a pure tone of e.g. 200 cps and the other to an equally loud tone of 203 cps, a distinct beating is heard. If the frequency difference is reduced from 3 to e.g. 1 cps a rotating tone image is heard by some observers though not by all of them. The beat itself is best heard at about 3 cps difference in frequency. It is different from a monaural beating between two equally loud tones of 200 and 203 cps in that the monaural beat passes from maximum loudness through zero and then again to maximum loudness and so on, whereas the binaural beat never reaches zero loudness. Still it can be clearly heard in the whole range between 90 and 800 cps. From 90 cps downwards a sensation of fulness is added to loudness, confusing the estimations by the test subjects. Between 800 and 850 cps audibility shows a sudden drop, keeping constant in that reduced state up to 1100 cps whereafter a rapid decline follows, down to complete disappearance at 1500 cps, beyond which frequency no beats can be produced any more, whatever loudness level is tried. This behaviour is schematically represented in Fig. 2, where the qualifications "good", "moderate", "poor" and "zero" indicate the audibility of the beats. These measurements have been done with four trained test subjects; their estimations were practically the same, in as far as these qualifications can be compared at all.

Audibility of Binaural Beats as a Function of Loudness Level

The audibility of binaural beats depends upon the amount of loudness modulation. It is of interest to know this amount of modulation brought

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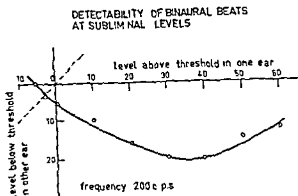
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I 3 Tl e l or ler l ne for tl e au lil ılıty of binaural beats if one ear is presented with a sul liminal l as a functi n of the level in the contralateral ear The curve is symmetrical with respect to tl last e l line

Audibility of Binaural Beats Below Threshold

Lehnhardt (1961) demonstrated the audibility of binaural beats if one of the signals was at subthreshold level In the same publication he described the detectability of a signal in noise it appeared that for both forms of bi naural stimulation (beats and noise) the detectability was 20 db better than for a monaural situation

We were able to confirm his results on binaural beats Furthermore we studied their audibility if one of the signals was below monaural threshold and the other above monaural threshold In Fig 3 the minimum subthreshold level in one ear is plotted as a function of the superthreshold level It ap pears that there is an optimum audibility of binaural beats if the level in one ear is between 30 and 40 db above threshold then the signal in the other ear which produces a just noticeable binaural beat reaches a minimum intensity level of 20 db below threshold These measurements were per formed with pure tones between 140 and 300 cps

This phenomenon amazing as it is in demonstrating the subthreshold activity of the peripheral organ of hearing has a strong relationship with the detectability of tone pulses in the presence of a constant background of a continuous tone the frequency of which being the same as used for the pulse (Derbyshire & Groen 1959) If the pulse level of the pure tone (e g 500 or 1000 cps) was maintained at the constant level of 10 db above thresh old the detectability of that pulse as a function of its duration depended upon the level of the constantly sounding tone *This in itself* is no miracle, but it appeared that the background tone could be reduced to 25 db below threshold in the monaural situation (pulse and background in the same ear) and to 1 5 db in the binaural situation (the pulse being presented to one ear ...

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perc ... that is considerably facilitated by a subthreshold sti

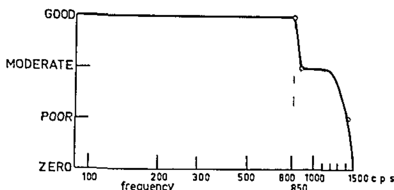


Fig. 9. The audibility of binaural beats is a function of frequency. The qualities good, moderate, poor and zero denote the detectability of the loudness modulation.

about by interference of the volleys. The same four test subjects have been asked to compare the binaural loudness modulation with a monaural one, the magnitude of which could be adjusted. The instrument used (designed and manufactured in our laboratory workshops) allowed presetting of all parameters involved so that by switching from binaural to monaural presentation the total loudness impression could be made to be the same. The frequency constancy of the oscillators was excellent, so was their output.

It appeared that in the frequency range between 90 and 800 cps the estimated binaural loudness modulation was about 2 db between maximum and minimum loudness. This value is different from the binaural loudness summation of two equally loud tones: above threshold a 6 db loudness increase is usual, whereas a 3 db addition takes place near threshold. The binaural beat produces a modulation which is less than both types of addition. This would suggest that the state of activation effected by binaural stimulation by two beating signals is at any time increased as compared to monaural stimulation by one of the two signals alone, even when the binaural beat passes through a minimum. This is proven when during a very slow binaural beat one of the signals is switched off: the loudness of the remaining signal is far less than the binaural loudness, be it at a maximum or even at a minimum. Actually it is surprising that there is almost no difference between the two loudness reductions: switching off one signal when the beat passes through a maximum or through a minimum sounds almost the same. In order to have some idea about this relationship, binaural loudness at the two extremes was compared with the monaural one. It appeared that when the binaural beat went through a maximum, the fall in loudness when one signal was switched off amounted to somewhat more than a factor of 2, whereas the fall from the minimum situation resulted in a factor of practically 2. It is very difficult to have these estimations in numbers. Far more observations would be necessary to obtain definite values.

beats can be heard at subthreshold levels in one ear, the other ear receiving a superthreshold tone or even a subliminal one this would point to a subthreshold activity of the peripheral organ of hearing

ZUSAMMENFASSUNG

In Fortsetzung der Arbeiten von Lane (1925) und Lehnhardt (1961) wurde das Phänomen der binauralen Schwebungen weiter studiert Das Verhalten der Schwebungen als Funktion der Frequenz deutet auf drei wesentlich verschiedene Gebiete hin optimale Wahrnehmbarkeit zwischen 90 und 800 Hz, weniger wahrnehmbar zwischen 850 und 1100 Hz, schnell verschwindende Wahrnehmbarkeit von 1100 bis 1400 Hz und totaler Ausfall ab 1500 Hz Auf dem Gebiete bester Wahrnehmbarkeit ist die Lautheit der binauralen Schwebungen vergleichbar mit einem etwa 2 db modulierten monauralen Sinustone Die binauralen Schwebungen können in einem Ohre verfolgt werden bis 20 db unter die Schwelle wenn in dem anderen Ohre der Schallpegel oben oder nahe an der Schwelle fixiert wird

RÉSUMÉ

Le phénomène des battements binaurales était étudié en poursuivant le travail de Lane (1925) et Lehnhardt (1961) Le comportement des battements comme fonction de la fréquence indique qu il y a trois régions différentes audibilité optimale de 90 à 800 cps audibilité reduit de 850 à 1100 cps diminuant rapidement de 1100 à 1400 cps disparition totale à partir de 1500 cps Dans la région d audibilité optimale la sonorité des battements binaurales est comparable à celle d un son monaural modulé de 2 db environ Les battements binaurales sont audibles jusqu à un niveau de 20 db au dessous du seuil dans une oreille pourvu que le niveau dans l autre oreille soit au dessus ou près du seuil

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Dept of Otolaryngology Utrecht State University
Utrecht The Netherlands

DISCUSSION

I B[illegible] We were able to confirm Mr Groen s statements, that is that binaural beats are better or exclusively detected within a limited band of frequencies between 200 and 1200 cps This fact leads us to think that the anatomical level where binaural beats take place must be very low along the central auditory pathway, just about or a little above the cochlear nuclei where the neuron units still respond with a 1 1 ratio to the incoming stimulus This may prove important from the clinical point of view

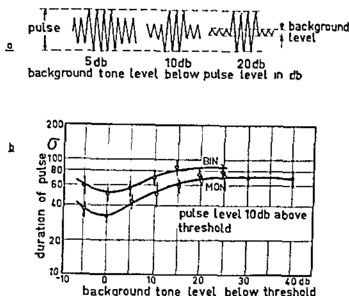


FIG 4a Level of continuous background tone in db below pulse level, this one being kept constant If the pulse tone would be continued for, say 2 sec, a 10 db tone level above threshold would be obtained *b*, *MON*, background and pulse in one ear presented as in (*a*) The duration of the pulse, necessary to produce a just audible tonal sensation, passes through a minimum when background and pulse have the same intensity The effect of the background tone goes on far below threshold, even down to −20 db *BIN*, in this situation the background tone is presented to one ear and the pulse to the other ear In general the trend is the same as in *MON*, but the facilitation ends asymptotically at −15 db

mulus in the other ear This again points to the possibility of peripheral and lower central activities at levels far below threshold

The quality of the binaural beat changes if one of the signals attains sub threshold values If one starts near threshold in both ears the beating is readily heard If we keep the level in one ear at say 30 db above threshold and we lower the level of the tone in the other ear gradually, the beating changes into a 'pulling' quality One locates the sound image in one ear (the one with the 30 db level), but this sound image is pulled periodically out of it in the direction of the centre of the head This is not a beating signal in the proper sense of the original meaning, but as the extreme case of a gradually changing quality, the term 'beat' is maintained

By looking at Fig 3, one can see that there is a chance of cross hearing through the head, the level difference being of the order of *40 to 50 db or* more In order to eliminate every possibility of cross hearing, the head phones were replaced by telephone receivers of the insert type (e g of a *hearing aid*) We *found no difference in* behaviour with the insert receivers beating went on at subthreshold levels as before

CONCLUSION

The phenomenon of binaural beats must have its origin in the neural mechanism of volleys interfering at a common group of synapses Binaural

EXPERIMENTAL STUDIES ON SOUND TRANSMISSION IN THE HUMAN EAR

V. Function of Stapedial Prosthesis

H. C. Andersen, C. C. Hansen and E. B. Neergaard
Aarhus, Denmark

From the Department of Otolaryngology, University of Aarhus

The transmission of sound in the ear in post mortem human temporal bones was measured before and after insertion of stapedial prosthesis of different material. It is shown that the increasing weight of the prosthesis does not improve the transmission in the high frequency range. Exposure to violent sound results in permanent transmission loss. The cause of this was identified in microscopic examination as a dislocation of the prosthesis, and is shown in a film.

The remarkable improvements of hearing following stapedectomy are not infrequently accompanied by a pronounced and inexplicable high tone loss.

John Shea (1963) has attempted to avoid this high tone loss by the use of a stapedial prosthesis the weight of which was increased by insertion of a piece of steel. The motive was that the ordinary polyethylene prosthesis represents a reduced mass as compared to the normal stapes and this reduction of weight is considered responsible for the hearing loss.

From an acoustical point of view it is relevant to perceive that the above mentioned high tone loss could possibly be caused by changes in mass, rigidity and friction, changes which might be compensated for by choice of a suitable prosthesis.

In order to throw light on this interesting and important question we have made some experiments to investigate what influence changing physical properties of the prosthesis may have upon the transmission of sound through the middle ear. These experiments have been made on human temporal bones removed *post mortem*.

In a previous paper (196…
on an experimental pr…
transmission of sound … uction system from the external ear canal through the ossicular chain and the labyrinth to the round window could be recorded in a frequency range of 125 cps–3200 cps. Having recorded the transmission characteristic of the intact middle ear, the stapedial arcade was removed through an opening in the tegmen of the tympanum. Prosthesis

Furthermore, we were able to demonstrate that the area of beats is much narrower in binaural than in monaural hearing In binaural hearing we can listen to two clear different tones with no beats or thrill superimposed where the tones differ in frequency by 10 %, while in monaural hearing the difference must be as great as 18 % That proves further that a basic difference must exist between peripheral beats and the central ones, the origin of the former being mainly physical, while that of the latter is mainly bound to neuronic activity and refractoriness

J J Groen (Reply) I am glad to hear that Prof Bocca came to the same results as we have The reason for the sudden drop in audibility of binaural beats beyond 800 cps must be due to a sudden loss of coherence of the volleys because of the refractory period of the conducting nervous mechanism I am eager to hear more about the application of the method of binaural beats on patients with disorders of the neural pathways I am interested in the measurements on pitch difference in mon and binaural situations as presented by Bocca We have the same experience in *the binaural situation the two tones keep their pitch, so two* pitches can be discerned at the same time, whereas in the monaural presentation there is only one pitch, being the algebraic mean of the two pitches

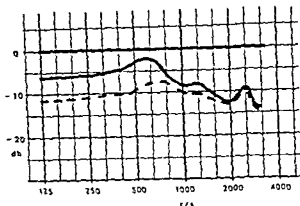


Fig. 2 Transmission in ear with a stapedial prosthesis before and after exposure to violent sounds

changes have proved quite reversible and no permanent damage has been found

In corresponding experiments on ears after prosthesis implantation a similar nonlinearity could be shown, but frequently irreversible damages in the transmission system occurred, as shown in Fig 2 and Fig 3

Fig 2 represents the transmission with a steel prosthesis compared with the preoperative transmission (0 db line) and the transmission at the same input level after exposure of the ear to violent sound In Fig 3 the output following a stepwise increase and decrease of the input tone at 25 cps is shown To the left preoperative and to the right after insertion of a stapedial prosthesis

Direct inspection through the microscope revealed a process which certainly causes nonlinearity and at the same time one could follow the progress of the noise injury at very high sound pressures it was evident that the prosthesis did not follow the movements of the incus Furthermore, the prosthesis sometimes performed rotating and jumping movements and occasionally a dislocation occurred from these violent vibrations, which were

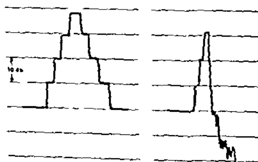


Fig 3 Output signal following stepwise increase and decrease of input level at 25 cps before and after insertion of a stapedial prosthesis

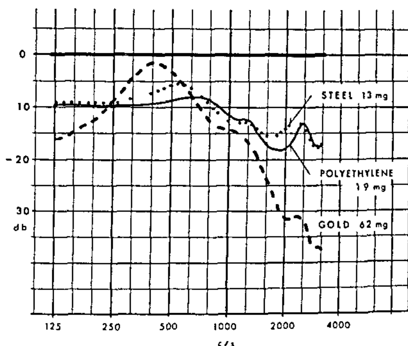


Fig. 1. Transmission of sound before and after insertion of prosthesis of polyethylene, steel or gold.

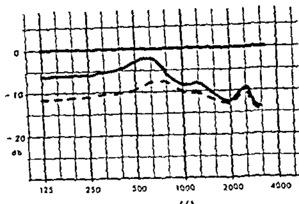
types resembling those used in Shea's stapedectomy have in succession been inserted as a replacement of the stapedial arcade. Various prosthesis materials have been used, viz. a polyethylene tube 1.9 mg, one of steel 13 mg and a prosthesis of gold 62 mg. The mass of the normal stapes is about 4 mg of which the arcade represents about 2.5 mg.

In all these experiments the prosthesis has been placed in identical positions, the end resting on the middle of the stapedial footplate. The insertion of a prosthesis was followed by a recording of the transmission characteristic.

The results appear from Fig. 1. As abscissa is used the frequency, while the ordinate represents the transmission of sound. It means that the zero db line corresponds to the normal transmission and each of the three curves represents the transmission of sound through the conduction system with the type of prosthesis indicated. It will be clear that the transmission in case of polyethylene and steel is practically the same, whereas the gold prosthesis yields a considerably poorer transmission. Only the frequency range about 500 cps shows a moderate improvement of transmission, presumably on account of some resonance phenomenon.

The conclusion is that we have *not* been able to give experimental support to the assumption made by John Shea that addition of mass to the prosthesis should prevent the occurrence of high tone loss at least up to 3200 cps.

In previous experiments we have measured the ratio of output to input sound level at increasing input levels in normal temporal bones, and in several cases a lack of proportionality—termed nonlinearity—was demonstrated at input sound levels exceeding 100 db. However, these functional



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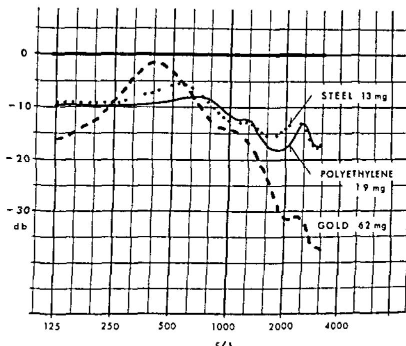


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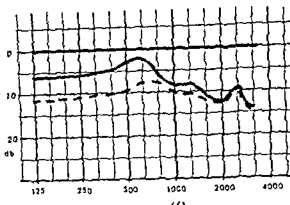


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Fig 3 Output signal following stepwise *increase* and decrease of input level at 25 cps before an l
thes s

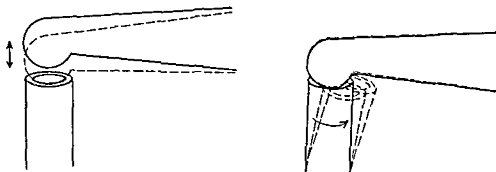


Fig 4 Behavior of a polyethylene stapedial prosthesis during violent sound exposure (shown in the film)

particularly clearly visible at the low frequencies (Fig 4) These phenomena can be seen in a film which was taken through the microscope

The observations show that exposure to violent sound may cause noise injuries in a middle ear which incorporates a prosthesis

(Demonstration of a film)

ZUSAMMENFASSUNG

Vor und nach Anbringung von Steigbügelprothesen, verschieden an Gewicht, wurde die Übertragung von Schall im menschlichen Ohr, *post mortem*, gemessen Die Untersuchung ergab, dass Gewichtzunahme keine Besserung der Übertragung hochfrequenter Tone zur Folge hat Im Falle heftiger Schallbelastungen wurde Nicht-Linearitat festgestellt, und bisweilen irreversible Reduktion der Übertragung Die Beobachtung durch das Mikroskop ergab, dass im Falle grosser Schallbelastungen Dislokation der Prothese entstehen kann Die Erscheinung wurde verfilmt

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Dept of Otolaryngology University of Aarhus, Denmark

DISCUSSION

M Portmann Je tiens à féliciter le Dr Andersen car il semble posséder là une méthode valable pour la contrôle de l'appareil de transmission Peut il utiliser cette méthode pour contrôler la perte d'impédance procurée par la technique du « piston »?

En effet cette méthode du « piston » systématiquement utilisée par certains auteurs doit être sérieusement étudiée

Le contact direct entre la columelle et les liquides cochléaires sans interposition risque à long terme de provoquer une atteinte de l oreille interne du fait qu'aucune impédance n'est opposée aux vibrations graves et intenses même longtemps après

Je suis un peu anxieux qu'un pourcentage important des maldes systématiquement opérés par « piston » depuis 3 ans développent dans 10 ou 20 ans des surdités cochléaires irremédiables du fait de cette perte de l'impédance stapédienne. Pouvoir contrôler expérimentalement la technique du « piston » serait donc très utile.

U. Siirala: I want to congratulate Prof. Andersen for his beautiful film. In our hospital in Helsinki we have used either a polyethylene prosthesis or stapedial crura for sound conduction in stapes. According to our experience it does not matter whether a polyethylene prosthesis or stapedial crura is used because the improvement of hearing is almost the same.

G. Herberts: The impedance of the ossicular chain is dependent not only on the ossicles but also on the action of the stapedius muscle. Its action is like a high pass filter. We have tried in a series of cases of stapes op. to save the tendon, both with the techniques of interposition and with stapedectomies. It is possible to save the tendon using the Schuknecht technique too.

After all these types of operation you get an increased discrimination loss, when tested in the presence of noise. But in the cases with a saved tendon the loss of discrimination will not be so marked.

H. C. Andersen (Reply) to M. Portmann: I can answer that it should be possible to measure the effect of the piston method. From a physiological point of view the method of Portmann is superior to the method of Shea because it keeps the contact between incus and stapes also during heavy sound exposure.

WEITERE HISTOPATHOLOGISCHE VERÄNDERUNGEN DES INNENOHRS BEI OTOSKLEROSE

L. Rüedi
Zürich, Schweiz

Aus der Otorhinolaryngologischen Klinik der Universität Zürich
(Direktor: Prof. Dr. L. Rüedi)

In Otoskleroseställen ist bisher nur ausnahmsweise eine senso-neurale Degeneration des Cortischen Organs nachgewiesen worden. Auch die Knochenneubildung in der Scala tympani im Zusammenhang mit Otoskleroseherden wird nur selten beobachtet. Demgegenüber finden sich in der Nähe von Otoskleroseherden, welche das Endost der Labyrinthkapsel durchsetzen und hier direkt ans Ligamentum spirale grenzen, recht häufig Veränderungen der Stria vascularis in Form einer umschriebenen Vermehrung der Gefäss-*Schlingen und einer Wucherung des Stria-Epithels*. Diese Stria-Wucherung entsteht allem Anschein nach infolge einer Zirkulationsstörung im Bereich des Ramus cochleae der arteria auditiva interna. Diese Zirkulationsstörung wird durch den Blutbedarf des aktiv wachsenden Otoskleroseherdes verursacht. Es stellt sich die Frage, ob diese umschriebenen Veränderungen der Stria vascularis und die im hochgradig aktiven Abschnitt des oberen Spiralligamentes (Spoendlin & Balogh) auftretenden Veränderungen der Blutzirkulation die Funktion des Innenohres beeinflussen können.

Am Otosklerose-Symposium in Detroit im Jahre 1960 hat A. Glorig an Hand von statistischen Gehöruntersuchungen von Ohrgesunden und von *Otosklerosepatienten das Vorkommen einer otosklerotischen Innenohr*schwerhörigkeit abgelehnt. An dem in Chicago vom 25.2. bis 1.3.63 stattgehabten Workshop on Reconstructive Middle Ear Surgery behandelte Carhart dasselbe Thema und kam dabei zu einem völlig anderen Ergebnis. Nach der Meinung von Carhart ist die Auswertung der statistischen Resultate *durch Glorig zu beanstanden*. Auch auf Grund dieses Materials ist eine Beteiligung des Innenohrs infolge der Otosklerose feststellbar. Dann zeigte Carhart eine Reihe von Fällen mit rasch *fortschreitender reiner Schallperzep*tionsschwerhörigkeit, die durch eine sogenannte cochleäre Otosklerose verursacht sein soll. Carhart vermutet toxische Schädigungen durch Otoskleroseherde, welche die endostale Kapselschicht ersetzen und dadurch in direkten Kontakt mit dem Endolymphraum gelangen. Als Coreferent habe ich die in *Detroit schon gezeigten* Innenohrveränderungen, welche in 9 funktionell und histologisch untersuchten Fällen feststellbar sind, nochmals kurz erwähnt. In 7 *Felsenbeinen von 4 Otosklerosepatienten*, welche eine ausgesprochene Perzeptionsschwerhörigkeit aufwiesen, wurden eindeutige histo-



Abb. 1 (52) 3 Vertikalschnitt durch das ovale Fenster. Otoskleroseherd ersetzt die endostale Kapselschicht. Wucherung der benachbarten Stria vascularis.

logische Veranderungen in der Schnecke gefunden. In 4 von diesen Felsenbeinen ist ein Zerfall des Cortischen Organs in der basalen Schneckenwindung begleitet von einer aufsteigenden Degeneration der zugehörigen nervösen Elemente vorhanden. In den 3 ubrigen Felsenbeinen dieser Gruppe fehlt das Cortische Organ in der basalen Schneckenwindung. In 9 Felsenbeinen von Otosklerosepatienten haben wir ausserdem Neubildungen von lamellarem Knochen beobachtet, welche stets in der Scala tympani der basalen Schneckenwindung lokalisiert sind. Der neue Knochen tritt auf z. B. in Form von osteoiden Säumen an der Ansatzstelle des Ligamentum spirale oder in Form einer Enostosis am Rand des runden Fensters, oder es wird das Lumen der Scala tympani durch grosse lamellare Knochenblocke weitgehend ausgefullt. Alle diese endostalen Neubildungen von lamellarem Knochen entwickeln sich regelmassig an der Oberflache eines aktiven Otoskleroseherdes, welcher die normale endostale Labyrinthkapselschicht ersetzt, so dass der Krankheitsherd an den Perilymphraum angrenzt.

Wir sind zu dem Schluss gekommen, dass die Otosklerose neben der Stapesankylose, dem Verschluss des runden Fensters, auch eine Atrophie der sensoneuralen Innenohrelemente und eine Knochenneubildung in der Scala tympani verursachen kann.

Heute kann eine weitere Veranderung des Innenohrs mitgeteilt werden, die zum Unterschied von den gezeigten Seltenheiten viel haufiger, d. h. in 22 Fallen von insgesamt 37 Fallen mit otosklerotischer Stapesfixation gefunden worden ist. Um die Moglichkeiten und die Gefahr der Stapedektomie zu beurteilen, ist dem vorderen unteren Rand des ovalen Fensters, dieser

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Abb. 3. 6(3. 5. Lymphatische Leukaemie. Wucherung der Stria vascularis

Schwellung der Stria vascularis. Zwei stark erweiterte Kapillaren sind eingehüllt in vermehrte epitheliale Elemente.

Umschriebene Striawucherungen sind also nicht spezifisch für die Otosklerose, sie kommen aber am häufigsten im untersten Bereich des Ductus cochlearis vor, in der Nachbarschaft eines Otoskleroseherdes am vorderen unteren Rand des ovalen Fensters, der hier die endostale Kapsel durchsetzt und ans Ligamentum spirale grenzt.

In der Folge haben wir in 13 von 37 Fällen ähnliche Striaveränderungen auch in den oberen Schneckenwindungen gefunden, stets ebenfalls in der Nachbarschaft von Otoskleroseherden, welche direkt ans Ligamentum spirale anstossen (Abb. 4, 5).

Wie entwickelt sich die umschriebene Striawucherung in der Nachbarschaft eines das Endost durchbrechenden Otoskleroseherdes?

Zur Beantwortung dieser Frage ist daran zu erinnern, dass die Blutversorgung der Stria vascularis bekanntlich durch den Ramus cochleae arteriae auditivae internae erfolgt (Abb. 6. Schema der Blutversorgung aus dem Handb. der Hals-Nasen-Ohrenkrankheiten. Denker und Kahler. Bd. 6, S. 343). Von dem in der Basis des Ligamentum spirale am Knochenrand verlaufenden Randgefäss zweigen arterielle Schlingen zur Stria vascularis ab. Das venose Blut wird von hier aus in die Spiralblattvene abgeführt. Der Ramus cochleae arteriae auditivae internae versorgt ausserdem die normalerweise sehr anspruchslose endostale Labyrinthkapsel. Ein wachsender Oto... ...t ein eigenes in sich geschlossenes Gefäss-System



Abb. 2. Stärkere Vergrösserung der Abb. 1

Lieblingsstelle der Otosklerose besondere Beachtung geschenkt worden. Dabei sind dort, wo der otosklerotische Knochenumbau auch auf die endostale Kapsel übergegriffen hat, im benachbarten Ductus cochlearis umschriebene Veränderungen der Stria vascularis festgestellt worden.

Diese Striaveränderungen sind histologisch durch eine umschriebene Erweiterung und eine Vermehrung der Kapillaren und ausserdem durch eine in diesem Bereich vorhandene Wucherung der epithelialen Striaelemente charakterisiert. Das normalerweise flache Polster der Stria ist verbreitert und wölbt sich stellenweise in Form eines umschriebenen Buckels oder in Form mehrerer gefässreicher Papillen ins schmale Lumen des Ductus cochlearis vor. Derartige Striaveränderungen finden sich z. B. bei einem 59j. Patienten (Abb. 1, 2).

Man erkennt im Vertikalschnitt durch das ovale Fenster, das Promontorium und durch das Ende der basalen Schneckenwindung einen otosklerotischen Umbau des vorderen unteren Fensterrandes. Der otosklerotische Knochen ersetzt die endostale Schicht und grenzt ans Ligamentum spirale. Im Ductus cochlearis findet sich in der Stria vascularis eine kugelige Schwellung. In stärker Vergrösserung (Abb. 2) handelt es sich um erweiterte bluthaltige Kapillaren, welche von einem breiten Saum aus Striaepithelien umgeben werden.

Zur Kontrolle dieser Striaveränderungen sind 40 Felsenbeine von ohrgesunden Fällen durchgesehen worden. In 2 Fällen haben wir ähnliche Striaveränderungen *gefunden*.

Einmal handelt es sich um eine Schädelbasisfraktur mit einer Mittelohrblutung. Der zweite Fall (Abb. 3), ein 60j. Mann, hat an einer lymphatischen Leukaemie gelitten. Man erkennt im Vertikalschnitt durch das ovale Fenster eine papilläre

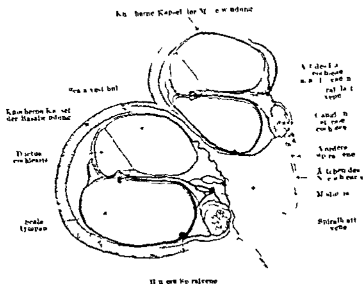


Abb 79 Schnitt durch die Basal und Mittelwindung der Schnecke mit Einzeichnung der Gefaße (Nach SHALTER 12)

Abb 6 Blutversorgung der Schnecke

das an verschiedenen Stellen aus dem alten Gefass System der Labyrinth kapsel entspringt und wieder in die schon vorhandenen Labyrinthkapsel venen einmundet

Die uns interessierende Beziehung zwischen einer Striawucherung in der Pars caeca des Ductus cochlearis und einem Otoskleroseherd am vorderen unteren Rand des ovalen Fensters lasst sich an Hand einer Schnittserie im Fall einer 60j Frau rekonstruieren (Abb 7 9)

Die zu besprechenden Schnitte verlaufen alle durch das ovale Fenster und durch das Ende des Ductus cochlearis in der basalen Schneckenwindung

Schnitt 330 Ein aktiver Otoskleroseherd durchsetzt den vorderen unteren Fensterrand Im Ductus cochlearis erkennt man eine polypos ins Lumen vorspringende Wucherung der Stria vascularis mit einem erweiterten Gefass, umgeben von einem breiten Saum aus Epithelzellen Nahe dem Rand des Otoskleroseherdes liegt im Ligamentum spirale ein erweitertes Gefass

Im Schnitt 320 liegt dieses sehr weite Gefass direkt am otosklerotischen Knochenrand und unmittelbar anstossend findet sich im kranken Knochen ebenfalls ein weites Gefasslumen

Im Schnitt 318 ist schliesslich ein weites Gefasslumen sichtbar, das zum Teil noch im ganz schmalen Ligamentum spirale und zum Teil schon im Bereich des otosklerotischen Knochens liegt

Die im vorhergehenden Schnitt sichtbaren Gefasslumina sind demnach Querschnitte einer Gefass Schlinge, die aus dem Ligamentum spirale in den otosklerotischen Knochen verlauft



Abb. 4. 75j. ♀. Otosklerosherd ersetzt die endostale Labyrinthkapsel in der 2. Schneckenwindung. Knochenneubildung an der Ansatzstelle des Ligamentum spirale. Wucherung der benachbarten Stria vascularis.



Abb. 5. [illegible]j. [illegible]. Aktiver Otosklerosherd durchbricht die endostale Labyrinthkapsel in der Schneckenwindung an der Ansatzstelle des Ligamentum spirale. Deutliche Verbreiterung der gesamten Stria vascularis.



Abb. Derselbe Fall wie Abb. 7 und 8. Übergang des erweiterten Gefässes aus dem Ligamentum spirale in den Otoskleroseherd.

Der otosklerotische Umbau in der endostalen Kapselschicht benötigt Blut. Der Herd wächst mit Hilfe eines eigenen Gefässystems, das aus einem schon vorhandenen arteriellen Ast und zwar in dieser Gegend aus dem Ramus cochleare der Arteria auditiva interna entspringt. Das venöse Blut aus dem Otoskleroseherd fliesst wieder an einer nicht bestimmbaren Stelle in die Spiralvene ab. Durch diese Anzapfung eines Gefässes—welches bis dahin hauptsächlich die Stria vascularis versorgt hat — zugunsten eines blutbeanspruchenden Otoskleroseherdes entsteht allem Anschein nach in der benachbarten Stria vascularis eine lokalisierte Zirkulationsstörung entweder in Form einer arteriellen Hyperaemie oder vielleicht auch in Form einer venösen Stauung. In der betroffenen Zone werden die Striagefässe erweitert und die epithelialen Stria-Elemente vermehren sich infolge der vermehrten Durchblutung.

Es stellt sich die Frage, ob durch diese Striawucherung die Produktion der Endolymphe verändert wird, so dass dadurch die Funktion des Innenohrs in Mitleidenschaft gezogen werden könnte. Nachdem unsere histologisch verarbeiteten Fälle leider nicht audiometriert worden sind, muss diese Frage vorläufig offenbleiben. Immerhin erscheint nach den Untersuchungen von Spoendlin & Balogh Jr. eine Beeinträchtigung der Innenohrfunktion im Falle einer otosklerosebedingten Zirkulationsstörung im vestibularen Abschnitt des Ligamentum spirale zum mindesten möglich. Spoendlin & Balogh haben nach intravitaler Inkubation der Cochlea eine besonders starke ... einen aeroben Stoffwechsel im Corti



Abb. 7. 65j. ♀. Otosklerosherd ersetzt die endostale Labyrinthkapsel an der Ansatzstelle des Ligamentum spirale. Wucherung der Stria vascularis. Im Ligamentum spirale erweitertes Gefäss.



Abb. 8. Derselbe Fall wie Abb. 7. Erweitertes Gefäss im Ligamentum spirale unmittelbar an der Oberfläche des Otosklerosherdes.

Aus dieser Reihenfolge verschiedener Einzelbilder ergibt sich eine vaskuläre Verbindung zwischen der Striawucherung und dem otosklerotischen Herd über dem Ramus cochleae arteriae auditivae internae.

Folgende Entstehungsmöglichkeiten der Striawucherung kommen in Betracht:

DISCUSSION

J Simson Hall He thought that it might help to explain many of the changes in hearing which at present were difficult to understand in the otosclerotic

He asked his opinion regarding the age of the bone which he described as new for as far as Dr Hall could see there were small indications of activity

M Arslan Two questions are put to Prof Ruedi (1) As it is known that the vessels of the otosclerotic focus when they are investigated with the hystochemical methods reveal severe troubles of the mesenchyme of the vessel walls, have been examined by Ruedi researches with the same methods the vessel of the stria vascularis too?

(2) How can the Ruedi s findings agree with the anatomical well known fact that the vascularisation of the inner ear (art auditive interna) is strictly separated from the vascularisation of the bone labyrinth capsule?

H Engstrom To the interesting communication of Prof Ruedi it may be commented that it is amazing how careful studies always can reveal important new findings To the question of new and old bone we may add that modern methods of X ray microradiography permit a rather exact way of defining the density of calcium and also to a certain extent the age of bone In some lantern slides the structure of otosclerosis in the stapes were shown as seen with X ray microscopy

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SUMMARY

Sensori-neural degeneration of the organ of Corti has been demonstrated in otosclerosis on rare occasions New bone formation within the scala tympani in relation to foci of otosclerosis is likewise rare On the other hand, deposits of otosclerosis *involving the labyrinthine capsule in close proximity to the spiral ligament*, are very commonly associated with changes in the stria vascularis These take the form of a circumscribed increase in the vascular loops and a proliferation of the epithelium of the stria It appears that this strial proliferation probably occurs as a result of a circulatory disturbance in the region of the cochlear branch of the internal auditory artery *The circulatory disturbance is caused by* the vascular demands made by the actively growing otosclerotic deposit It still remains to be proved whether these circumscribed changes in the stria vascularis and the circulatory changes due to the highly active upper portion of the spiral ligament (Spoendlin & Balogh) could affect the function of the inner ear

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Otorhinolaryngologische Klinik
der Universität Zürich, Schweiz



Fig. 1. Osteitis deformans. Female aged 65 years. Skull. The bone has been irregularly absorbed and correspondingly replaced by loose vascular fibrous tissue. Numerous osteoclasts are attacking the trabeculae, while rows of osteoblasts are also applied to the bone here and there. The trabecula below and to right of centre shows a slight mosaic pattern. Haematoxylin and eosin. × 90 diam.



Fig. 2. *Osteitis deformans.* Male aged 69 years. Skull. The enlarged spaces are occupied by loose fibrous material. The bone is made up of plates of variable size and shape and so exhibits a characteristic mosaic pattern. Osteoclasts are applied to the bone in space at top right. Haematoxylin and eosin. × 130 diam.

THE HEALING PROCESS IN OTOSCLEROSIS

I SIMSON HALL and R F OGILVIE
Edinburgh, Great Britain

The purpose of this short communication is to show the similarities i healing processes in the temporal bone and in some diseases includin otosclerosis

If bone is damaged by disease or by trauma, repair is undertaken an it may be assumed that such appearances as are noted are due to the pro cesses involved in healing Variations encountered may well be caused b the special characteristics of the bone undergoing repair

The mode of healing of fractures of normal bone is too well known t require emphasis and we confine ourselves here to the effects of damag to abnormal bone and its repair

Otosclerosis has been compared at one time or another to each of th well known bone dystrophies, *osteitis fibrosa*, Paget s disease, and osteo genesis imperfecta

We have emphasised the differences between these diseases and thei similarities in respect of age, sex incidence, distribution and blood chemica changes In this instance we are concerned solely with the histologica characteristics of the bone

In osteitis fibrosa we have a process in which there is widespread destruc tion of bone by osteoclasis As the process extends we note evidence o repair in the form of osteoblasts which by the production of osseomucin may lay down new bone It is characteristic of this disease that one side of a bony trabecula is being formed by osteoblasts while the other is being absorbed by osteoclasts

The whole process indeed resembles the appearances we are accustomed to examine in the early or active stage of otosclerosis

Osteitis deformans, or Paget s disease, has similar characteristics histologi cally Bone is removed by osteoclasis and replaced by the action of osteo blasts (Fig 1) Like osteitis fibrosa both processes can be observed continuing at the same time In osteitis deformans, however, the process is slower and healing is seen in a more advanced state which gives rise to the mosaic pattern of Schmorl (Fig 2) It would seem therefore that this appearance indicating healing is also a sign of chronicity or a long standing condition

Osteogenesis imperfecta, whether in the general skeleton or in the temporal bone, presents the same characteristic osteoclastic destruction (Fig 3) Osteoblastic deposition finally culminates in the healing and consolidation of bone after puberty As this disease is recognised as due to an osteoblastic insufficiency it appears that unstable or unsatisfactory bone is liable to be resorbed wherever laid down

It seems therefore that in all these diseases bone is repaired in a similar

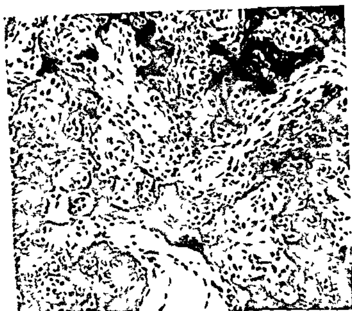


Fig 4 Otosclerosis Male aged 19 years with deafness for 9 years Footplate of stapes The bone is abnormally cancellous from enlargement of the Haversian canals The fibrous material filling the interstices is loose and cellular and includes vessels ranging to sinuses Osteoclasts are absorbing the trabeculae here and there while osteoblasts are laying down new bone in several areas The trabeculae are thin and irregular and show a variation in quantity and distribution of their osteocytes Haematoxylin and eosin 150 diam



Fig 5 Osteogenesis imperfecta Female aged 16 years Femur The original cortical bone to left is abnormally thin and has been fractured centrally New cancellous bone streams to right from the fractured site into the medullary cavity The interstices are occupied by loose highly vascular fibrous tissue while rows of osteoblasts are frequently applied to the trabeculae Haematoxylin and eosin 40 diam



Fig. 3. Osteogenesis imperfecta. Stillborn female pig. Otic capsule with facial nerve bottom right. The bone is strikingly cancellous. The fibrous tissue occupying the interstices is generally loose and vascular but is much more cellular towards right than above left. The trabeculae are thin and laminated. Their substance is being attacked by numerous osteoclasts while their surfaces are frequently layered over with osteoblasts. Small deposits of active marrow are noted in the less cellular fibrous tissue. Haematoxylin and eosin. × 55 diam.

fashion. This we have shown is characteristic of otosclerosis also. If the conclusion is correct that these changes represent the replacement of unsatisfactory bone, any further necessity for healing such as a fracture of the bone should cause no special change or new appearance but healing *should proceed as before*.

In two instances footplates which were fractured during a mobilisation operation were subsequently extracted during stapedectomy.

Under the operating microscope the evidence of fracture in such cases is frequently clear but in the sections healing is proceeding as before in spite of the fracture. The histological appearances are those of healing bone such as we are accustomed to see in such cases (Fig. 4). This means that no additional changes are brought about by the fracture for it occurs through bone which is already in a process of repair and the fracture cannot be separately identified because the processes are identical.

For comparison we show a section of the healing not of a temporal bone but of a fractured long bone in a case of osteogenesis imperfecta and if it is compared with osteogenesis imperfecta in the temporal bone and again with otosclerosis we do not believe that they can be distinguished one from the other on purely histological grounds (Fig. 5). They are in fact the same process, namely bone under repair. Injury gives rise to exuberant bone

AGE REGULARITIES IN THE FERTILITY OF WOMEN AND THEIR RELATION TO THE DEVELOPMENT OF OTOSCLEROSIS

ANTONÍN PŘECECHTĚL
Prague, Czechoslovakia

1500 women admitted to the obstetric clinic of Prof. Luka (Prague) and taken in order as they were admitted to the clinic were divided into three groups each containing 500 women. By subtracting the average time of their pregnancies, i.e. nine months, the age at conception was found for the three groups. A curve was drawn for each group in such a way that the age of the women at conception was noted on the abscissa and the number of cases at the given age on the ordinate.

All three curves (the first as basic one, the other two as controls) show a remarkable similarity in a number of particulars; it may therefore be assumed that they are the expression of certain biologic regulations in ontogenesis. We may call them curves of relative age fertility of woman.

These curves were compared with the curves derived from the age of incidence of the probable beginning of 100 cases of otosclerosis arranged as they were admitted in the clinic. This group contained 73% of woman and 27% of man. From these subgroups of both sexes two curves were set up separately.

The curves between themselves and in comparison with the fertility curve show from the point of view of age characteristic agreement on the one side and also differences on the other side.

These findings may contribute to the determination of the various critical phases of age for the development of different disturbances of the metabolism in the blood and in the labyrinthine capsule in otosclerosis and thus to the solution of the etiopathogenetic prevention and treatment of otosclerosis.

A retrospective view on research carried out hitherto on the problem of otosclerosis shows a remarkable success of surgical treatment but etiopathogenetic research has still not advanced so far as to be able to procure a new basis for successful prevention and conservative treatment. It therefore will be necessary to deepen this research branch further especially with the aid of various biological and mainly biochemical methods.

In this paper we want to report on the aims our research in the given question is directed to: in continuation of the biologic research of Hermann Swoboda, who on analysis of pedigrees observed in many studies the rhythm of life in various physiological processes and diseases. Swoboda detected very frequently a rhythm of *seven years* in these processes. This ontogenetic research may be elaborated also in another way.

formation at the site of fracture, which is in complete contrast with the poor bone structure generally This provides a possible explanation for the profuse production of bone which is called hyperostosis We have shown *this previously to be a very early stage in otosclerotic bone change* and for which there has been up till now no rational explanation This profuse formation of new bone is in keeping with the rapidity with which fractures in osteogenesis imperfecta are known to heal

We are beginning to understand clearly the nature of the changes in the bone in otosclerosis, but the deficiency in our knowledge lies in the lack of proof regarding the cause of the necessity for replacement of bone

We have drawn attention elsewhere to the similarities between osteogenesis imperfecta and otosclerosis and have suggested that as in osteogenesis imperfecta the primary defect is in the osteoblast This seems the more likely as in some of our material the bone changes have commenced at a very early age

It is important to ascertain whether this vulnerability of the bone to reconstructive change is a genetic defect only, or whether it can be caused by other factors which may come into action at different times throughout life

From our study of bone taken from patients of widely differing ages we incline to the view that the essential changes of otosclerosis commence at a very early age though they may be accelerated, or possibly retarded by circumstances encountered within the early decades of life

14 Moray Place Edinburgh 3 Scotland

The illustrations were prepared by the Photographic Department under Mr T C Dodds I R P S

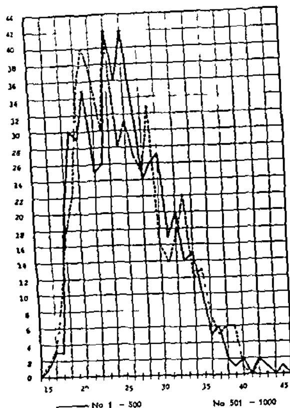


Fig 2

Figure 1 presents the basic curve It starts at the age of 15 with one case and ends at the age of 45 It may be divided into four parts the first, ascending part, from 15–21 years, *the second* part, forming the peak, from 21 26 years, the third, descending part, from 26–40 years, the fourth, residual part, with interruption from 41–45 years

The control curves have quite a similar course Figure 2 presents the first control curve it is marked as interrupted line, the basic curve by a full line

Figure 3 represents the second control curve marked as an interrupted line and the basic curve as a full line

Already a general aspect of the basic curve and of the two control ones shows a remarkable similarity of all three curves, which in their total present the following characteristic features The beginning at the age of 15, 15, 16 years, the peak is reached at the age of 21, 21, 19 years, the peak ends at the age of 30, 29, 30 years There are two maxima for each peak The termination of the curves is at the age of 45, 42, 42

The great similarity of all three curves is given by the almost simultaneous age at the beginning the almost equal length of the peak, the two maxima upon it, with almost the same number of cases for the maxima

Multiples of number seven are found not unfrequently at the beginning

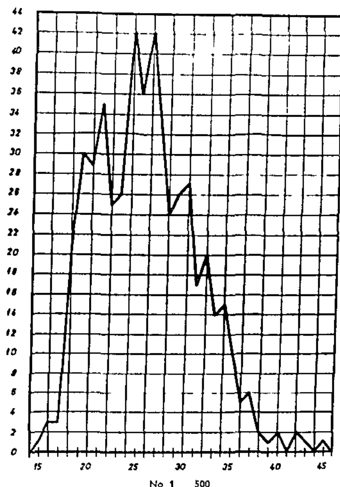


Fig. 1

It is known from biological statistics, that fertility may be defined as the number of live born children per 1000 women in their reproductive age from 15–45 years.

It is also possible to set up a curve from any larger number of births from a certain group according to the age of the women, which demonstrates the relative frequency of birth rates in the various years of the reproductive age of the women. This curve may also be called a curve of relative fertility. A series of 1500 women admitted to the obstetric clinic of Prof. Lukaš of the Charles University at Prague and taken in the order as they were admitted to the clinic, was analysed in order to obtain such a curve and to determine its characteristics. This series was divided into three groups, each containing 500 women: 1–500, 501–1000, 1001–1500. The average time of duration of their pregnancies was subtracted from their age at delivery, i. e. nine months, and thus the age at conception was found for the whole series of women. A curve was drawn for each group in such a way, that the age of the women at conception was noted on the abscissa and the number of cases at the given age on the ordinate.

The curve of group I was called the basic one, the other two (II and III) were controls.

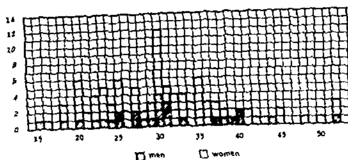


Fig 4

in both sexes occurs at the same age (15 years) and for both sexes the curves end also at the same age (at 52 years) A further agreement is to be noted for the age of the maximum number of cases for both sexes (at 30 years of age)

But there appear also differences in the curves The female one is compact, showing a mass incidence from 20 to 35 years The male one, on the contrary, shows a marked decrease of incidence from the 32nd to 35th year, at the age of 35 there appears even a complete gap in the curve, whereas *in women, on* the contrary a considerable increase occurs at this age

These *otosclerotic* curves show also signs of the rhythm of seven and of its multiples

The female curve shows a marked increase from 15 21 years, regular *oscillations* at a certain general level from 21 years 28 years *and then* a steep rise to the maximum (at 30 years) which keeps to the same high level *till the* age of 35 years even after a certain decrease, *and finally a further* declining decrease

In men the curve starts at 15 years the *greatest fall* is at 35 years and after that the incidence shows *irregular* gaps

Comparing the fertility curves in woman with the otosclerotic *ones* an agreement is to be noted in that fertility *and the first* symptoms of the development of otosclerosis *(in both sexes)* appear usually at *the same age, i e* at 15 years However there are also differences

The maximum fertility in women lies between their 19th and 25th *year* The maximum incidence of otosclerosis *is at 30* years (for both sexes) The maximum incidence *of otosclerosis* in woman therefore is shifted to a

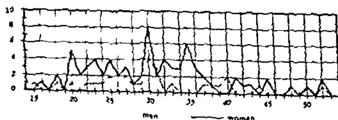


Fig 5

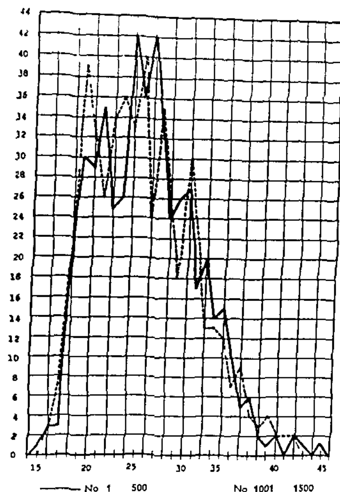


Fig 3

on reaching the peak, the intervals of the maxima spread over six years the end of the curve is at the age of 42 (2 ×) With regard to the fact that the characteristics of all curves are very similar in a number of features, we may assume with great probability that they are the expression of certain biologic regulations in the ontogenesis of woman

We compared the curves derived from the ages of incidence of the probable beginning of 100 cases of otosclerosis with these curves of relative age valence of the fertility of women, taking data from case histories of a series of patients in the order as they were generally admitted to the ORL clinic This group contained 73 % woman and 27 % men

Out of both groups a common columnar diagram was set up (Fig 4) but separately for both sexes Women are represented by white squares, men by hatched squares

The diagram demonstrates that the number of men and women is different that, however, their age distribution on the abscissa agrees partly and partly it differs also Those agreements and disagreements are especially well marked on the curves

In Fig 5 the female curve is in full line, the male one as interrupted line Agreements on both curves (men and women) the beginning of incidence

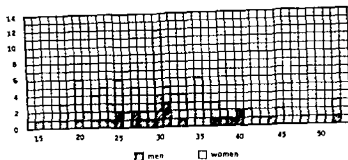


FIG 4

in both sexes occurs at the same age (15 years) and for both sexes the curves end also at the same age (at 52 years) A further agreement is to be noted for the age of the maximum number of cases for both sexes (at 30 years of age)

But there appear also differences in the curves The female one is compact, showing a mass incidence from 20 to 35 years The male one, on the contrary, shows a marked decrease of incidence from the 32nd to 35th year at the age of 35 there appears even a complete gap in the curve, whereas in women, on the contrary, a considerable increase occurs at this age

These otosclerotic curves show also signs of the rhythm of seven and of its multiples

The female curve shows a marked increase from 15 21 years regular oscillations at a certain general level from 21 years–28 years and then a steep rise to the maximum (at 30 years), which keeps to the same high level till the age of 35 years even after a certain decrease, and finally a further declining decrease

In men the curve starts at 15 years, the greatest fall is at 35 years and after that the incidence shows irregular gaps

Comparing the fertility curves in woman with the otosclerotic ones an agreement is to be noted in that fertility and the first symptoms of the development of otosclerosis (in both sexes) appear usually at the same age, i e at 15 years However, there are also differences

The maximum fertility in women lies between their 19th and 25th year The maximum incidence of otosclerosis is at 30 years (for both sexes) The maximum incidence of otosclerosis in woman therefore is shifted to a

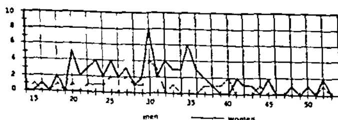


FIG 5

higher age than the maximum of fertility, to a period, when considering their fertility, the biologic valence of women starts already to decline continuously.

The upper limit of the occurrence of otosclerosis at 52 years is explained by the beginning of climacterium and with some shifting towards the higher age. This explanation for the man, however, is not possible, as a biological climacterium in man does not exist according to Belonoschkin.

It is known that many authors found hormonal and enzymatic disturbances of the protein, phosphor and calcium metabolism in the blood and the labyrinthine capsule in otosclerosis. Our research may contribute to the determination of the various critical phases of age for the development of these biochemical disturbances and thus to the solution of the etiopathogenetic prevention and treatment of otosclerosis, based upon ontogenetic observations.

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Malá Strana, Karmelitská 1, Prague 1, Czechoslovakia

ÜBER BASSTAUBHEIT

B. LANGENBECK
Bonn, Deutschland

Demonstrationen einiger Fälle, bei denen nach den audiologischen Befunden Basstaubheit angenommen werden kann. Es wird gezeigt, dass die tiefen Töne nur zum Teil durch ihre Obertöne zur Wahrnehmung kommen können und dass die neurophysiologische Erklärung Meyer zum Gottesberges die bessere ist.

Wir wissen, dass Diskanttaubheiten mit Steilabbruch der Hörkurve nach den hohen Frequenzen hin bei relativ gutem Gehör in den tieferen Tonlagen wie in Abb. 1 nicht so ganz selten sind. Sie kommen vor z. B. nach Schädeltraumen oder infolge degenerativer Prozesse. Man muss aber fragen: Warum beobachten wir nie das Pendant dazu, also Hörkurven mit gutem Gehör bei hohen Tönen und Steilabbruch nach den tiefen Tönen hin, also Basstaubheiten?

Gravendeel (1958) machte 1958 auf ein Krankheitsbild aufmerksam, das er als Basstaubheit bezeichnete und bei dem er völligen Ausfall der Hörfunktion in den tiefen Tonlagen annahm. Ich habe gleichartige Fälle beobachtet, z. B. Abb. 2, wo der Hörausfall links plötzlich erst vor ein paar Stunden bemerkt war und rechts seit acht Wochen bestand, beiderseits reine Schallempfindungsstörung, d. h. Knochenleitung = Luftleitung. Auch bei den mitgeteilten Fällen Gravendeels ist der Hörkurvenabfall wie in Abb. 3 nach den tiefen Tonlagen hin mehr oder minder flach auslaufend und bis zu den tiefsten Tönen hin werden noch Hörschwellen angegeben. Gravendeel erklärt dieses Verhalten damit, dass ja auch bei erloschenem Hörvermögen für tiefe Töne doch deren entotisch entstandene Obertöne (vielleicht verstärkt durch die Obertöne des Audiometers) zur Hörempfindung führen müssten, eine Erklärung, die meines Wissens auch Schubknecht ins Feld führte bei Tierversuchen, bei denen ihm eine isolierte Zerstörung der Schneckenspitze gelungen war (ca. 40 db Hörverlust!).

Den Beweis, dass dem so sein müsse, sah Gravendeel in einem Ausweichen der geräuschaudiometrischen Kurve nach grösseren Tonintensitäten hin im Bereich der tiefen Töne, genau wie bei meinem Fall Abb. 2. Natürlich mussten diese Töne viel grössere Intensität haben, damit die viel schwächeren Obertöne neben dem Geräusch gehört werden konnten.

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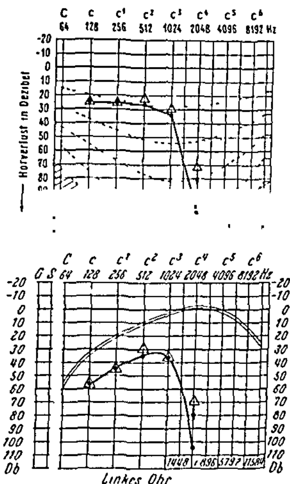


Abb 1 Diskanttaubheit nach Schadeltrauma Oben Horverlust Unten Absolutdarstellung

All das ist in meinem Fall, Abb 2 (Patient B H, Untersuchung am 10 5 1951), sehr schon zu sehen, der als ganz frisch entstandene Schwerhörigkeit besonderes Interesse verdient Der Horausfall auf dem linken Ohr war seit einigen Stunden als plotzlicher Horsturz (sudden deafness) bemerkt worden, auf dem rechten Ohr bestand die Schwerhorigkeit seit zwei Monaten Auf beiden Ohren Knochenleitung = Luftleitung, also reine Schallempfindungsstorung Betrachten wir zuerst das linke Ohr Die Schwellenkurve (oben) entspricht der eben gegebenen Beschreibung Von c³ ab nach den hohen Tonen hin altersentsprechend normales Gehor Von c³ ab nach den tiefen Tonen flach auslaufender Steilabfall Das Gerauschaudiogramm liegt von c³ an nach oben normal im Niveau der Gerauschkulisse von 30 db, nach den tiefen Tonen hin weicht das Gerauschaudiogramm aber tief nach unten (also den grosseren Tonintensitaten) hin aus

Auf dem rechten Ohr ahnlicher Befund, nur ist offenbar in den zwei Monaten des Bestandes auch in mittleren und hohen Tonlagen eine Schadigung eingetreten Der Fowler-Test auf diesem Ohr ist positiv, wie es Gravendeel auch fordert

Über den interessanten klinischen Verlauf des demonstrierten Falles werde ich am Schluss berichten Zuerst mochte ich einige Bedenken aussern, namlich erstens hinsichtlich der Erklarung Gravendeels solcher Befunde als durch das Horen der entotischen Obertone entstanden, und zweitens mochte

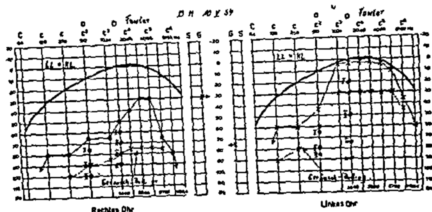


Abb. 2. Schwerhörigkeit links seit einigen Stunden, rechts seit ca. 8 Wochen bestehend.

ich vor schematischer Auffassung solcher und ähnlicher Befunde als Basstaubheiten warnen.

Erstens habe ich nun untersucht, ob sich die beobachtete Hörkurve des linken Ohres auf Grund von Obertonbildung erklären lässt. Wir haben die Obertöne subjektiv nach der Methode der best beats genau so wie Fletscher (1948) bestimmt, dabei aber die Audiometertöne benutzt, ohne Aussiebung der objektiven Obertöne. Wie Abb. 3 zeigt, ist der gemessene Obertongehalt etwas grösser (ca. 10 db) als bei Fletscher, offenbar weil doch die Audiometertöne noch einen geringen Prozentsatz Obertöne enthalten, was ja bekannt ist. Wie die rechte Seite der Abb. 3 zeigt, wäre die Schwelle c¹ auf dem linken Ohr des Patienten von Abb. 2 vielleicht durch Obertöne erklärbar, sicherlich aber nicht die Schwelle bei c, die mit Sorgfalt wiederholt bestimmt wurde. Die Schwellen der Obertonreihe sind, wie man sieht, sicher unterschwellig für den Patienten gewesen.

Wir haben die Obertöne bei normalen Versuchspersonen bestimmt. Es ist anzunehmen, dass diese normalen Verhältnisse auch bei dem Patienten Abb. 2 zutreffen müssen. v. Békésy hat bekanntlich gezeigt, dass die entotischen Obertöne infolge Wirbelbildung in dem Schneckenliquor entstehen müssen. Viskositätsänderungen sind aber bei der erst einige Stunden bestehenden Hörstörung nicht anzunehmen, so dass auch die entotische Obertonbildung wie beim Normalen sein dürfte.

Meyer zum Gottesberge teilte mir mündlich mit, dass er eine andere Erklärung für wahrscheinlicher halte, und ich schliesse mich seiner Meinung nach dem Bisherigen an. Abb. 4 zeigt nach Umzeichnung in die audiometrische Darstellungsweise eine Messung aus Tierversuchen von Katsuki (1962), bei denen Einzelfasererregungen im Hörnerven bestimmt und nach Schwellen ausgewertet wurden. Das Empfindlichkeitsmaximum liegt bei den tiefen Tönen über die c³-Stelle hinweglaufenden Wander der Basilarmembran erregen aber immer die c³ Faser im Hörnerv nach mit Vergleich mit der Hörkurve (rechte Seite Abb. 4) zeigt

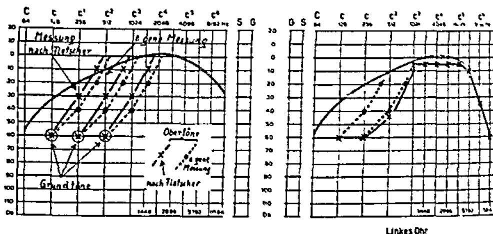


Abb. 3. Linke Hälfte: Reihe der mit Audiometer gemessenen entotischen Obertöne bei Normalen. Rechte Hälfte: durch Obertöne wird der Verlauf der Schwellenkurve von Abb. 1 nicht erklärt.

dass sich mit diesem Modell eine recht gute Erklärung der Hörschwellenform ergibt, wenn man eine völlige Basstaubheit für c und c^1 annimmt.

Die Form der geräuschaudiometrischen Kurve aus Abb. 2 (linkes Ohr) lässt sich vielleicht durch das Hören von Obertönen erklären, denn bei 80 bis 90 db ist der Obertongehalt nach eigenen Bestimmungen erheblich grösser, und die Linien der Obertonreihe in Abb. 3 links verlaufen sehr viel flacher.

Zweitens glaube ich nicht, dass ein Ausweichen der geräuschaudiometrischen Kurve nach grösseren Tonintensitäten im Tieftongebiet immer eine Basstaubheit im Sinne Gravendeels beweisen muss. Wir haben im Laufe der Jahre verschiedene andere, häufig vorkommende Momente *kennengelernt*, die *ein* solches *Ausweichen* der geräuschaudiometrischen Kurve anderweitig erklären.

Abb. 5 linkes Ohr zeigt am 8.11.1934 die Verhältnisse bei einer seit 5 Jahren bestehenden Schwerhörigkeit, die anfangs mit periodischen Schwindelanfällen schwankend, seit Jahren aber konstant geblieben war. Positiver

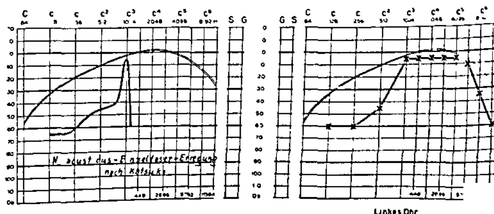


Abb. 4. Die Katsuki-Kurve gibt eine gute Erklärung der Schwellenkurve.

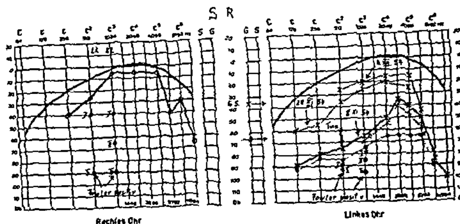


Abb. 5. Typischer Menière-Fall nach 5jähriger Krankheit mit Erholung des Gehörs. Ohrengeräuschen im Tieftongebiet.

Fowler-Test bei c^2–c^3. Die geräuschaudiometrische Kurve bei 60 db Geräusch verläuft unter dem Hörmaximum (2000–6000 Hz) *normal*.

Das Ausweichen der geräuschaudiometrischen Kurve nach unten bei c^2–c^3 vor der Hörschwellenkurve ist hier aber zweifellos durch das *in* diesem Bereich angegebene Ohrgeräusch (Tinnitus) bedingt und nicht im Sinne einer Basstaubheit nach Gravendeel zu werten. *Subjektive Ohr*geräusche verschlechtern ja einerseits das Schwellengehör in dem betroffenen *Gebiet*, addieren sich aber andererseits zu dem statistischen *Geräusch* des Audiometers, so dass die geräuschaudiometrische Kurve *in dem be*troffenen Gebiet nach höheren Tonintensitäten ausweicht (Langenbeck, 1963).

Nach *operativer Sanierung* einer doppelseitigen chronischen Sinusitis erholte sich das Gehör unter Theophyllin-Traubenzucker-*Therapie in kurzer Zeit*, das Ohrgeräusch verschwand (vgl. Kontrollen Abb. 5 am 28.11. und 4.12.1961).

Abb. 6: ein Fall, der in der Kindheit einen Schädelbruch gehabt hatte, trotzdem aber *immer gut hörte*. *Seit einem Vierteljahr* hatte er über wechselnde Schwerhörigkeit auf dem linken *Ohr* zu klagen, verbunden mit Ohrgeräusch. Der Fowler-Test bei c^3 schien negativ zu sein. Die geräuschaudiometrische Kurve *bei 60 db* Geräusch *liegt* von c^3 nach den hohen Frequenzen hin normal bei *60 db*, *ent*sprechend der Geräuschkulisse, weicht aber unter dem abfallenden Kurvenschenkel nach den tiefen Tönen hin stark nach unten aus. *Bei dem negativen* Fowler-Test konnte man an eine retrolabyrinthäre Störung *im Tiefton*bereich denken, die zugleich das Ausweichen der geräuschaudiometrischen Kurve nach höheren Tonintensitäten erklären *würde* (*pathologische* Verdeckbarkeit) (Langenbeck 1963). Auffällig ist aber das *Ergebnis* der Readaptationsmessung (Kietz-Test). Wir messen die Readapta*tion nach* Durchmessen der geräuschaudiometrischen Kurve mit dem Geräusch, das nun durch Feinzeitschalter etwa

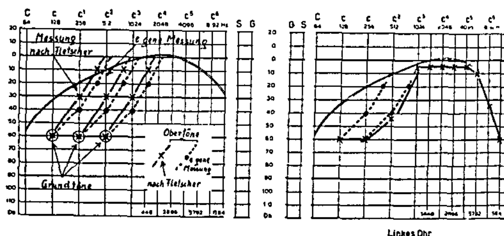


Abb 3 Linke Hälfte Reihe der mit Audiometer gemessenen entotischen Obertöne bei Normalen Rechte Hälfte durch Obertöne wird der Verlauf der Schwellenkurve von Abb 1 nicht erklärt

dass sich mit diesem Modell eine recht gute Erklärung der Hörschwellenform ergibt, wenn man eine völlige Basstaubheit für c und c¹ annimmt

Die Form der geräuschaudiometrischen Kurve aus Abb 2 (linkes Ohr) lässt sich vielleicht durch das Hören von Obertönen erklären, denn bei 80 bis 90 db ist der Obertongehalt nach eigenen Bestimmungen erheblich grösser, und die Linien der Obertonreihe in Abb 3 links verlaufen sehr viel flacher

Zweitens glaube ich nicht, dass ein Ausweichen der geräuschaudiometrischen Kurve nach grösseren Tonintensitäten im Tieftongebiet immer eine Basstaubheit im Sinne Gravendeels beweisen muss Wir haben im Laufe der Jahre verschiedene andere, häufig vorkommende Momente kennengelernt, die ein solches Ausweichen der geräuschaudiometrischen Kurve anderweitig erklären

Abb 5 linkes Ohr zeigt am 8 11 1954 die Verhältnisse bei einer seit 5 Jahren bestehenden Schwerhörigkeit, die anfangs mit periodischen Schwindelanfällen schwankend, seit Jahren aber konstant geblieben war Positiver

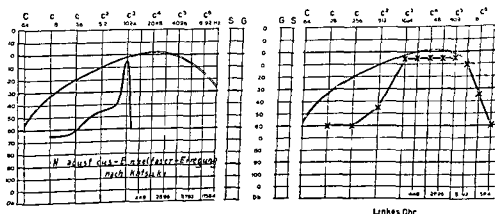


Abb 4 Die Katsuki Kurve gibt eine gute Erklärung der Schwellenkurve

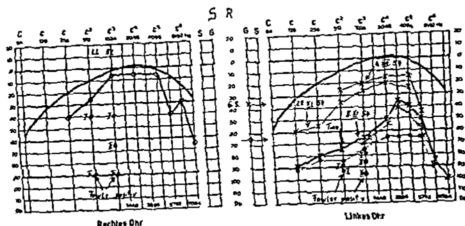


Abb 5 Typischer Ménière Fall nach 5jähriger Krankheit mit Erholung des Gehörs Ohrenrauschen im Tieftongebiet

Fowler Test bei c^2 c^3 Die geräuschaudiometrische Kurve bei 65 db Geräusch verläuft unter dem Hörmaximum (2000–6000 Hz) normal

Das Ausweichen der geräuschaudiometrischen Kurve nach unten bei c^2 c^3 vor der Hörschwellenkurve ist hier aber zweifellos durch das in diesem Bereich angegebene Ohrgeräusch (Tinnitus) bedingt *und nicht im* Sinne einer Basstaubheit nach Gravendeel zu werten Subjektive Ohrgeräusche verschlechtern ja einerseits das Schwellengehör in dem betroffenen Gebiet addieren sich aber andererseits zu dem statistischen Geräusch des Audiometers so dass die geräuschaudiometrische Kurve in dem betroffenen Gebiet nach höheren Tonintensitäten ausweicht (Langenbeck, 1963)

Nach operativer Sanierung einer doppelseitigen chronischen Sinusitis *erholte sich* das Gehör unter Theophyllin Traubenzucker Therapie in kurzer *Zeit das Ohrgeräusch* verschwand (vgl Kontrollen Abb 5 am 28 11 und 4 12 1954)

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in ½-sec-Rhythmus fur ca 70–80 Millisekunden unterbrochen wird, und be stimmen erneut die Tonschwellen in dem so rhythmisch unterbrochenen Gerausch (Kietz-Test, vgl Abb. 6) (Langenbeck, 1963) Wahrend der Kietz Test in den mittleren und hoheren Tonlagen sich gut von der gerauschaudio metrischen Kurve abhebt, also gute Readaptation beweist, klebt die Kietz Test-Kurve im Bereich c^1–c^2 vollstandig auf der gerauschaudiometrischen Kurve und zeigt damit stark pathologisch veranderte Adaptationsverhältnisse oder starke Horermudung bei 60 db Gerausch an Es ist also wahrscheinlich dass im Tieftonbereich eine traumatische Vulnerabilitat vorliegt, die schon bei der geringen Gerauschstarke von nur 60 db kurzzeitig anhaltende Horverschlechterung zur Folge hat (Mikrotrauma) (Langenbeck, 1963) Im gleichen Sinne sprach der *Schwellenschwundtest* Hier sprechen also die Gerauschaudiometrie einschliesslich Ermudungs- resp Adaptationsteste im Sinne einer Innenohrstörung, der Fowler-Test, den ich wegen der starken Traumatisierbarkeit des linken Ohres nicht fur ganz sicher halte, fur retro labyrinthare Störung

Die Vestibularisuntersuchung zeigte eine geringe, vorwiegend qualitative Unterer regbarkeit des linken Ohres, die andererseits aber auch als Hyperreflexie rechts ge deutet werden konnte, was nach Unterberger ja fur zentrale Storung im Bereich des linken Hypothalamus sprechen wurde Die neurologische Untersuchung hat bis jetzt keinen weiteren Aufschluss ergeben

Jedenfalls ist auch im Fall Abb 6 das Ausweichen der gerauschaudio metrischen Kurve nicht im Sinne einer Basstaubheit nach Gravendeel zu werten Es bieten sich einmal partielle retrolabyrinthare Storung, anderer seits mikrotraumatische Storung (Schwellenschwund) als Erklarung an

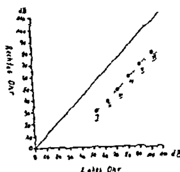
Es ist also in ahnlichen Fallen wie den hier gezeigten nötig, genau zu prufen, ob das Ausweichen der gerauschaudiometrischen Kurve sich nicht einfacher als Folge von Schwellenschwund, retrolabyrinthärer Storung oder als Folge von subjektiven Ohrgerauschen erklart, ehe man eine Basstaubheit im Sinne von Gravendeel annimmt

Bei dem zuerst demonstrierten Fall Abb 2 konnte die Readaptation nicht be stimmt werden, da der Kietz Test erst spater entwickelt wurde Es ist also unsicher, ob bei dem Fall Abb 2 nicht auch Schwellenschwund vorgelegen hat

Ich muss nun gestehen, dass wir seit 1958, wo wir regelmassig die in Frage kommenden Falle auf Schwellenschwund oder im Kietz Test prufen, typische Falle von Basstaubheit im Sinne Gravendeels nicht mehr gesehen haben Ich meine also, dass solche Befunde wohl sehr selten sind und, wenn uberhaupt, nur passager vorkommen Jedenfalls scheinen Basstaubheiten sehr viel seltener zu sein als Diskanttaubheiten

Liegt das vielleicht daran, dass die von der Schneckenbasis, also der Empfindung der hohen Tone dienenden Hornervenfasern aussen um den Hornerven herumgewickelt und deshalb Verletzungen mehr ausgesetzt sind als die im Innern des Hornerven zur Schneckenspitze laufenden Fasern?

Andererseits ist ja auch die fensternahe Schneckenbasis toxischen Ein-



Schwellenschwundtest bei C⁴ L nach 1' 20 dB absinkend dann > 1' constant

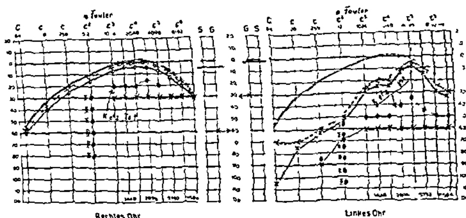


Abb. 6. Tiefton-Schallempfindungsstörung mit Ausweichen der geräuschaudiometrischen Kurve. Schwellenschwund im Tieftonbereich (Kietz-Test), retrolabyrinthäre Störung?

wirkungen infolge Diffusion durch die Fenstermembranen in viel stärkerem Masse ausgesetzt als die Schneckenspitze.

Weiter müssen wir berücksichtigen, dass alle Wanderwellen im inneren Ohr immer über die Schneckenbasis hinweglaufen. Traumatisch wird also die Schneckenbasis immer am meisten betroffen.

Pathogenetisch scheint es also so, als wenn die der Wahrnehmung der hohen Töne dienenden Elemente im Innenohr und Hörnerven am exponiertesten sind. Auf der anderen Seite ist aber zuzugeben, dass Ernährungsstörungen in der Schneckenspitze durch Verschluss der Endarterie besonders leicht möglich sein müssen, so dass wir das Vorkommen von Basstaubheiten erwarten müssen. Anhangsweise noch kurz einiges zum klinischen Verlauf jenes Falles Abb. 2, der mir sehr aufschlussreich im eben skizzierten Sinne scheint.

Ich stellte bei dem Patienten, der mich 1954 erstmalig aufsuchte, röntgenologisch einen rundlichen Schatten am Boden der linken Kieferhöhle über einem apicalen

im ½ sec Rhythmus für ca. 70–80 Millisekunden unterbrochen wird und bestimmen erneut die Tonschwellen in dem so rhythmisch unterbrochenen Geräusch (Kietz-Test, vgl. Abb. 6) (Langenbeck 1963). Während der Kietz-Test in den mittleren und höheren Tonlagen sich gut von der geräuschaudiometrischen Kurve abhebt, also gute Readaptation beweist, klebt die Kietz-Test-Kurve im Bereich c¹–c² vollständig auf der geräuschaudiometrischen Kurve und zeigt damit stark pathologisch veränderte Adaptationsverhältnisse oder starke Hörermüdung bei 60 db Geräusch an. Es ist also wahrscheinlich, dass im Tieftonbereich eine traumatische Vulnerabilität vorliegt, die schon bei der geringen Geräuschstärke von nur 60 db kurzzeitig anhaltende Hörverschlechterung zur Folge hat (Mikrotrauma) (Langenbeck 1963). Im gleichen Sinne sprach der *Schwellenschwundtest*. Hier sprechen also die *Geräuschaudiometrie einschliesslich Ermüdungs-* resp. *Adaptationsteste* im Sinne einer Innenohrstörung, der Fowler-Test, den ich wegen der starken Traumatisierbarkeit des linken Ohres nicht für ganz sicher halte, für retrolabyrinthäre Störung.

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Liegt das vielleicht daran, dass die von der Schneckenbasis, also der Empfindung der hohen Töne dienenden Hörnervenfasern aussen um den Hörnerven herumgewickelt und deshalb Verletzungen mehr ausgesetzt sind als die im Innern des Hörnerven zur Schneckenspitze laufenden Fasern?

Andererseits ist ja auch die fensternahe Schneckenbasis toxischen Ein-

SUMMARY

A number of cases is demonstrated in which according to audiometric results a low tone deafness must be assumed. As it appears low tones can only partially be perceived by their harmonics, and thus the neurophysiologic explanation by Meyer zum Gottesberge is more probable.

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Baumschulallee 29, Bonn, Deutschland

DISCUSSION

Meyer zum Gottesberge: Es scheint mir doch, dass durch die Untersuchungen von Herrn Langenbeck die Frage per exclusionem beantwortet ist. Wenn nachgewiesen ist, dass die Erscheinung durch endaurale Obertone nicht ausreichend erklärt werden kann, so muss man annehmen, dass bei Schädigungen des Apex der Cochlea durch die Wanderwellen Bezirke der Basilarmembran erregt werden, welche fensterwärts vor der Schädigung liegen. Dass eine solche Erregung tatsächlich stattfindet, beweisen die Ableitungen des Aktionspotentials von einzelnen Nervenfasern (Katsuki) eindeutig.

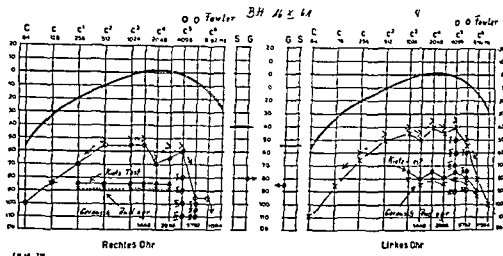


Abb. 7. Übergang der Hörstörung in typische Ménière-Schwerhörigkeit nach 7 Jahren.

Granulom fest bei negativem Ergebnis der Kieferhöhlenspülung. Ausserdem fand sich Osteochondrose der unteren Halswirbelsäule mehr als der Brustwirbelsäule. Vestibuläre Erscheinungen waren nur vorübergehend nachweisbar. *Das Gehör* besserte sich nach Zahnextraktion unter Tetracyclinschutz, andere Medikamente blieben wirkungslos.

7 Jahre später kam der Patient abermals in meine Behandlung, weil das *Gehör* sich in letzter Zeit wieder verschlechtert hatte. Er bot nun das typische Bild einer Ménière-Schwerhörigkeit, wobei allerdings die vestibulären Erscheinungen im Hintergrund standen. Das Audiogramm Abb. 7 zeigt gleichmässig über die Tonskala verteilten Hörverlust auf beiden Seiten. Das Geräuschaudiogramm verläuft im Niveau der Geräuschstärke, wie bei Innenohrstörung zu erwarten. Kein Ausweichen der geräuschaudiometrischen Kurven bei tiefen Tönen mehr wie in Abb. 2. Der Kietz-Test (Langenbeck, 1963) zeigt verlangsamte Readaptation an, ein Befund, wie wir ihn ebenso wie den Schwellenschwund (vgl. Abb. 6) fast regelmässig bei Ménièrestörungen sehen. Die Bodenverschattung in der linken Kieferhöhle war erheblich grösser geworden. Die Operation ergab einen grossen Bodenpolypen in der linken Kieferhöhle, unter dem sich reichlich rahmiger Eiter entleerte. Nach etwa 4 Wochen hatte sich das Gehör namentlich im Tieftongebiet erheblich gebessert.

Es hat sich also wohl um das Frühbild einer sich entwickelnden Ménière-Schwerhörigkeit in Abb. 2 gehandelt bei wenig ausgesprochenem Schwindel.

RÉSUMÉ

Démonstration de quelques cas d'une surdité des sons graves dans l'examen d'audiométrie.

Conclusions: les sons graves sont remarqués seulement en partie par leur sons harmoniques, la définition neuro-physiologique de Meyer zum Gottesberge est la meilleure.

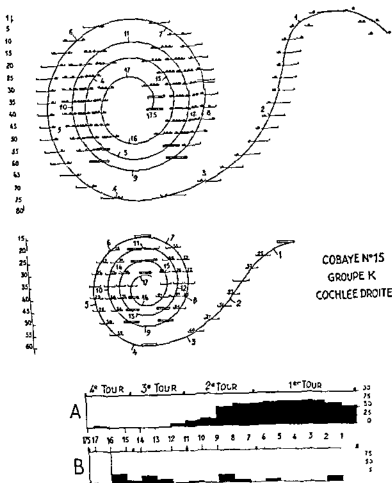


Fig. 1. Cobaye n° 15 groupe K. En haut reconstruction graphique de l'organe de Corti. Les cercles noirs dans chaque cupule représentent les cellules sensorielles présentes. Zones hachurées artefacts. Les chiffres représentent les distances en millimètres de la base à l'apex. Importantes lésions dégénératrices du premier et du deuxième tour. En bas reconstruction du ganglion spiral. Les gros chiffres correspondent à ceux du graphique de l'organe de Corti. Les petits chiffres sont ceux de la numération cellulaire. En A diagramme des destructions de l'organe de Corti. En abscisses les distances, en ordonnées les pourcentages de destruction. En noir les zones détruites. En B diagramme des destructions du ganglion spiral.

MOYENS ET MÉTHODES D'ÉTUDE

Lors de notre précédent travail (12) nous avions constitué un groupe de cobayes dit « groupe K (14 à 18) soumis à un traitement de Kanamycine seule – injection intramusculaire quotidienne 14 jours consécutifs de 400 mg par kg de poids et par jour. Chaque animal avait été sacrifié dix jours après la fin du traitement par perfusion fixatrice vitale endocardiaque. Les rochers avaient été immédiatement isolés, fixés, décalcifiés, déshydratés,

ÉTUDE EXPÉRIMENTALE DE L'ACTION ANTITOXIQUE DE CERTAINS ACIDES AMINÉS ET VITAMINES AU NIVEAU DES CELLULES DE L'ORGANE DE CORTI

MICHEL PORTMANN et JACQUES DARROUZET
Bordeaux, France

Les auteurs se demandent s'il ne serait pas possible, en administrant préventivement certains médicaments protecteurs, de réduire ou d'empêcher les lésions de l'oreille interne par les antibiotiques ototoxiques (Streptomycine, Dihydrostreptomycine et Kanamycine).

Ils expérimentent sur le cobaye, soumis à un traitement de Kanamycine, et montrent que, si l'administration de corticoïdes se montre assez décevante, un soluté composé de complexe vitaminique B et d'acides aminés s'est avéré capable de *protéger intégralement l'organe de Corti 6 fois sur* 10, et de réduire les lésions 1 fois sur 10, alors que la dose de Kanamycine *utilisée était 20 fois supérieure à la dose thérapeutique usuelle.*

INTRODUCTION

Grâce à des constatations cliniques et expérimentales, (4, 5, 6, 7, 8, 9, 10, 11, 12, 18, 19, 21, 22, 23, 24, 26, 27, 29, 30, 31, 32, 33, 34, 35, 38, 39, 41, 44, 45, 47, 49, 50), l'effet *ototoxique de certains antibiotiques* (streptomycine et Dihydrostreptomycine, Néomycine, Kanamycine) est actuellement bien connu. Il nous a paru intéressant d'essayer de freiner et si possible d'empêcher la destruction cellulaire ototoxique en administrant préventivement, en même temps que l'antibiotique toxique, un médicament supposé protecteur. Nous nous sommes arrêtés à cette attitude délibérément prophylactique car tout traitement à visée curative institué après la dégénérescence cellulaire nous a paru voué à un échec certain.

Comme protecteurs nous avons essayé:

1° *Le delta cortisone, dans l'hypothèse où un processus allergique pourrait* être invoqué comme cause de la destruction cellulaire.

2° L'association du complexe vitaminique *B et des acides aminés (méthionine*, histidine, tryptophane et citrate de choline), parce que ce mélange a été proposé comme traitement des surdités de perception, quelle qu'en soit l'origine.

Bien entendu, ces deux médicaments ne constituent pas une liste limitative. Ils ne représentent que le début d'une série d'essais systématiques actuellement en cours dont nous donnerons les résultats au fur et à mesure des examens anatomopathologiques.

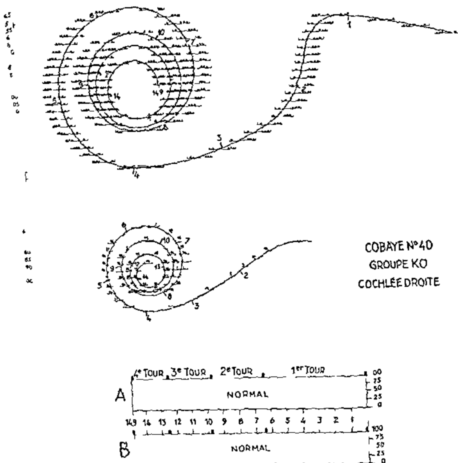


Fig 3

mètre par millimètre le pourcentage des cellules détruites (fig 1 2 3 diagrammes A)

La même méthode est appliquée à la reconstruction du ganglion spiral (fig. 1 2 3) Le chiffre inscrit dans les cupules représente le nombre de cellules comptées dans un champ arbitrairement fixé L'examen de ce graphique nous permet d'établir un diagramme des pourcentages de destruction selon la distance de la base à l'apex et d'établir une comparaison du dommage subi respectivement par les cellules sensorielles et les cellules ganglionnaires (fig 1 2 3 diagramme B)

Pour chaque cochlée nous disposons ainsi d'un dossier complet d'une sorte de fiche signalétique permettant l'appréciation rapide des lésions et des confrontations entre les différents individus et groupes

Dans le présent travail le groupe K (Kanamycine seule) a servi de groupe de référence et c'est par la comparaison des graphiques des groupes K et ...upes KD (Kanamycine delta cortisone) et KO (Kanamycine

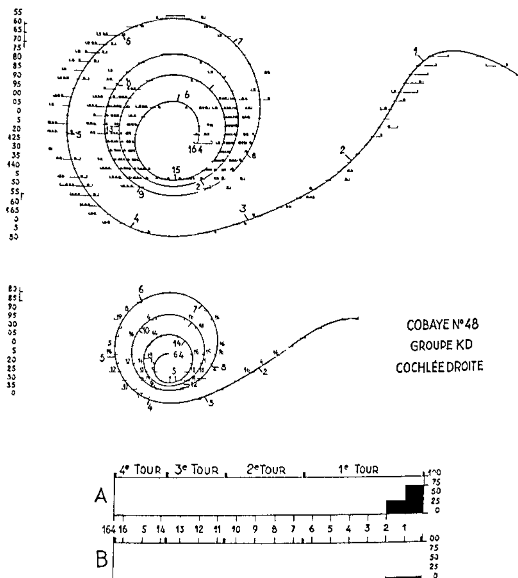


FIG. 2

inclus en celloïdine et coupés. Chaque coupe ayant reçu un numéro, nous avons pu reconstituer chaque cochlée suivant la méthode de Guild (20).

Chaque image d'organe de Corti est mise en place sur trame millimétrée à son emplacement exact et représentée par une cupule rectangulaire (fig. 1, 2, 3). Sur chaque cupule les 3 cellules ciliées externes et la cellule ciliée interne sont représentées par des cercles noirs si elles sont présentes. En cas de destruction elles ne sont pas représentées. La cupule reste vide. Cette représentation simple permet de prendre très rapidement une notion de l'importance et de la répartition des lésions. Une précision supplémentaire est apportée par la mesure au curvimètre des distances en millimètres de la base à l'apex = cette mesure permet de jalonner toute la longueur de la cochlée de repères millimétriques (fig. 1, 2, 3). Nous pouvons alors pour chaque oreille interne examinée établir un diagramme représentant milli

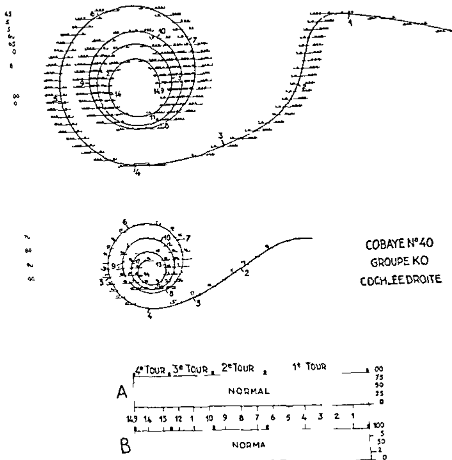


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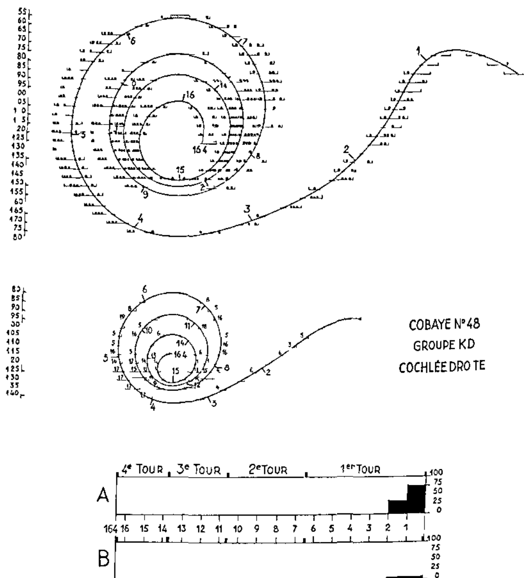


FIG. 2

inclus en celloïdine et coupés. Chaque coupe ayant reçu un numéro, nous avions pu reconstruire chaque cochlée suivant la méthode de Guild (20).

Chaque image d'organe de Corti est mise en place sur trame millimétrée à son emplacement exact et représentée par une cupule rectangulaire (fig. 1, 2, 3). Sur chaque cupule les 3 cellules ciliées externes et la cellule ciliée interne sont représentées par des cercles noirs si elles sont présentes. En cas de destruction, elles ne sont pas représentées = la cupule reste vide. Cette représentation simple permet de prendre très rapidement une notion de l'importance et de la répartition des lésions. Une précision supplémentaire est apportée par la mesure au curvimètre des distances en millimètres de la base à l'apex = cette mesure permet de jalonner toute la longueur de la cochlée de repères millimétriques (fig. 1, 2, 3). Nous pouvons alors pour chaque oreille interne examinée établir un diagramme représentant milli-

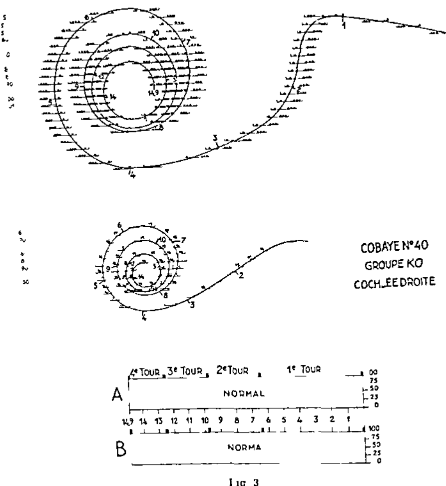


Fig 3

mètre par millimètre le pourcentage des cellules détruites (fig 1 2 3 diagrammes A)

La même méthode est appliquée à la reconstruction du ganglion spiral (fig 1 2 3) Le chiffre inscrit dans les cupules représente le nombre de cellules comptées dans un champ arbitrairement fixé L examen de ce graphique nous permet d établir un diagramme des pourcentages de destruction selon la distance de la base à l apex et d établir une comparaison du dommage subi respectivement par les cellules sensorielles et les cellules ganglionnaires (fig 1 2 3 diagramme B)

Pour chaque cochlée nous disposons ainsi d un dossier complet d une sorte de fiche signalétique permettant l appréciation rapide des lésions et des confrontations entre les différents individus et groupes

Dans le présent travail le groupe K (Kanamycine seule) a servi de groupe de référence et c est par la comparaison des graphiques des groupes K et des deux groupes KD (Kanamycine delta cortisone) et KO (Kanamycine

mélange vitamine acides aminés) que nous avons pu apprécier la valeur protectrice de la delta cortisone et des *amino acides*.

Les cobayes du groupe KD (*cob. n° 42 à 48*) ont reçu la même dose de Kanamycine que ceux du *groupe K* (injection quotidienne de 400 mg par kg poids et par jour pendant 14 jours) associés pour chacun d'eux à *une dose quotidienne d'un dixième de ml de suspension de delta cortisone soit* environ ½ mg de produit actif par jour.

Les cobayes du groupe KO (34 à 41) ont reçu le même traitement standard de Kanamycine mais dans le même temps ils recevaient par injection intramusculaire distincte un demi millilitre d'une solution de vitamines + acides aminés.

Les animaux des groupes KO et KD ont été sacrifiés comme ceux du groupe K 10 à 15 jours après *la* fin de l'expérimentation. *Les* techniques de préparation histologique et de reconstruction graphique appliquées ont été rigoureusement identiques. Les documents du *groupe* K d'une *part* des groupes KD et KO d'autre part sont donc parfaitement comparables.

RÉSULTATS

1° groupe K

L'organe de Corti

Les cellules sensorielles externes sont dégénérées en totalité au niveau du premier tour et de la moitié basale du deuxième. A leur place apparaît une structure réticulaire ou fibrillaire et l'on voit souvent à l'emplacement de *l'ancien pole supérieur des granulations sombres. Partout* la cellule sensorielle interne persiste apparemment intacte.

Au niveau des tours supérieurs les cellules nobles internes et externes persistent en totalité.

Quant aux structures de soutien nous avons noté quelques altérations: tendance à l'aplatissement des cellules de *Hensen* et de *Claudius* externes, aspect flou de leurs limites, présence de vastes lacunes cytoplasmiques. Par contre les piliers, la membrane basilaire, la membrana tectoria, la strie vasculaire paraissent intacts.

L'épaississement de la membrane de Reissner et l'exsudat fibrino hématique de la rampe vestibulaire que nous avons constatés sur certaines coupes nous paraissent imputables à un excès de pression lors de la perfusion.

Le ganglion spiral

Paraît normal à un examen superficiel. La numération cellulaire montre un déficit léger, beaucoup moins important que celui de *l'organe de Corti* (fig. 1 *A* et *B*).

Le labyrinthe postérieur

Ne présente aucune altération de structure bien caractérisée.

Au total *nous considérons* comme essentielle la destruction des cellules externes du 1er tour et de la moitié basale du deuxième. Cette règle peut subir

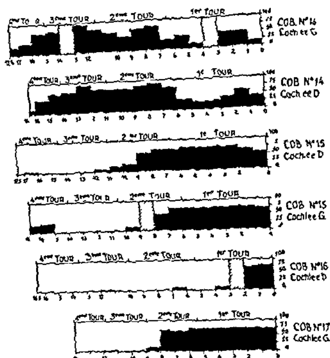


Fig 4

des variations individuelles mais elle est valable pour la majorité des cas comme le montrent les diagrammes etablis pour toutes les cochlees examinées diagrammes groupés fig 4

2° Groupe KD

Dans ce groupe de 8 animaux l un n a pas atteint le terme de l experimentation un autre avait une absence congenitale de cochlee Sur les 12 cochlees restantes 9 seulement étaient explorables en ra son l — teehn ~

auc ult

L organe de Corti

Les résultats sont rassembles dans le tableau de la fig 5

Sur les 9 cochlees reconstruites aucune n est exempte de lesions de cellules sensorielles

Pour 7 d entre elles les lesions sont a la fois peu intenses et peu étendues surtout puisqu elles ne depassent pas le 2eme millimètre (cochlees n° 43 45 46 48) Comme toujours elles intéressent les cellules sensorielles externes exclusivement et ne comportent aucun aspect histologique particulier Les

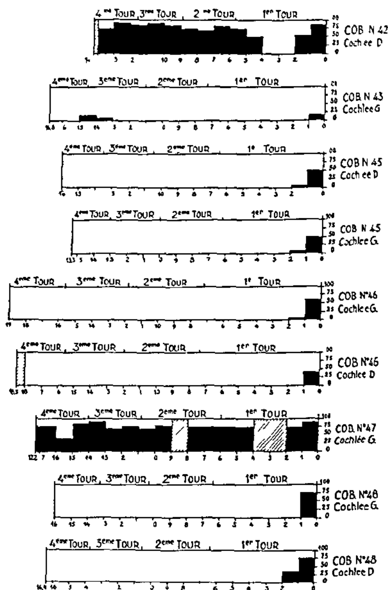


FIG. 5

structures de soutien sont peu modifiées et même dans les zones de dégénérescence elles conservent un aspect quasi normal.

Pour 2 cochlées (n° 42 et 47) les destructions sont au contraire très étendues intéressant la presque totalité des cellules externes à tous les niveaux de la cochlée.

Le ganglion spiral

On note une très légère diminution de la population cellulaire correspondant aux zones lésées de l'organe de Corti.

Le labyrinthe postérieur

paraît intact. Au total dans le groupe KD sur 9 cochlées reconstruites 7 ont des lésions de la partie initiale du tour basal, 2 ont des lésions extrêmement importantes étendues à toute la longueur de l'organe de Corti.

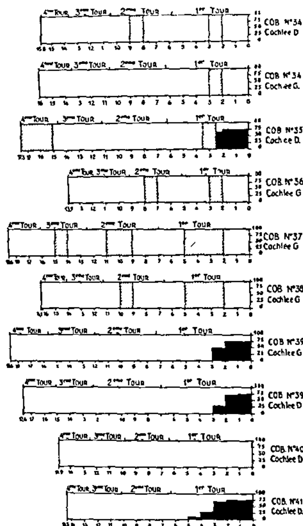


Fig 6

3° Groupe KO

Dans ce groupe comportant 8 animaux, donc 16 cochlées nos difficultés techniques ont fait que 10 cochlées seulement ont pu faire l objet d une interprétation indiscutable Les résultats sont groupés fig 6

L organe de Corti

Sur les 10 organes de Corti de ce groupe six ne présentent aucune lésion de dégénérescence au niveau de la « zone fragile », c est à dire le premier tour Certes la présence d artefacts representés sur les diagrammes par les zones hachurées, appelle quelques réserves, mais nous croyons que, étant donnée la topographie bien connue des lésions dégénératives qui siègent de

l'avis unanime des auteurs au niveau du tour basal, nous sommes en droit de considérer comme intact, comme respecté par l'agression médicamenteuse un organe de Corti dont les 2 premiers millimètres ne montrent aucun signe de dégénérescence.

A côté de ces six organes de Corti intacts, nous en voyons 4 qui ont subi des lésions dégénératives. L'aspect histologique est identique à celui constaté dans le groupe K, les cellules ciliées externes étant électivement détruites, mais la distribution topographique des lésions est sensiblement différente, puisqu'elle ne dépasse pas la moitié du 1er tour.

Le ganglion spiral

est normal quand il n'y a pas de lésions de la cellule sensorielle. Lorsqu'il y a dégénérescence des cellules nobles il existe un discret déficit cellulaire du ganglion dans le territoire correspondant.

Le labyrinthe postérieur

parait intact. Au total, l'examen histologique fait apparaître, dans le groupe KO, six fois sur dix, une protection intégrale de l'organe de Corti. Dans les 4 autres cas, l'étendue des lésions est considérablement diminuée par rapport à ce qui a été constaté dans le groupe K.

DISCUSSION ET CONCLUSIONS

Nous avons tenté de protéger l'oreille contre l'agression toxique en administrant préventivement certains médicaments, en partant de deux hypothèses simples.

1° S'il s'agit d'une agression allergisante, les corticoïdes doivent prévenir la dégénérescence.

2° S'il s'agit d'un trouble métabolique, et plus précisément d'une perturbation enzymatique, peut-être la vitaminothérapie, peu efficace lorsque la lésion est constituée, pourrait-elle être efficace à titre préventif.

Partant de ces hypothèses, nous avons essayé, concurremment avec la Kanamycine, la delta cortisone (Groupe KD) et le mélange complexe B plus amino-acides (Groupe KO).

L'examen de la figure 6 montre que pour 7 des 9 cochlées du groupe KD, les lésions sont nettement moins étendues que dans le groupe K. Certains organes de Corti de ce groupe semblent donc avoir été protégés. Mais deux autres (Cob 42 cochlée D, et cob 47 cochlée G) montrent des lésions plus importantes que celles du groupe K. Ce fait est troublant et rien ne nous permet d'en donner une explication valable. Les lésions préexistaient-elles? Sont-elles dues à la kanamycine, ou à la delta cortisone, ou à la conjonction des deux médicaments? Dans l'ignorance où nous sommes de la bonne interprétation à donner, *nous sommes obligés de conclure que des essais cliniques ne nous paraissent pas opportuns.*

Quant à la vitaminothérapie, il faut se garder sans doute autant de l'enthousiasme démesuré que du scepticisme tranchant et injuste.

La vitaminothérapie dans les surdités de perception n est pas une nouveauté Elle comporte des bases expérimentales Dès 1940, Covell cité par Fiori Ratti (17) créait expérimentalement des carences électives en divers facteurs vitaminiques et trouvait des lésions des cellules ciliées externes dans les carences B2 B6 et C des altérations du ganglion spiral dans la carence A Divers essais thérapeutiques eurent lieu diversement appréciés par les auteurs puis l on en vint à utiliser le complexe B et finalement en 1916 un soluté comprenant un complexe B associé à des acides aminés sous l impulsion de Hirschfeld Jacobson Jellinek (25) En France de la Farge (14 15) Lavergne (28) publièrent des observations de surdités de perception remarquablement améliorées par l association (complexe B + méthionine histidine tryptophane et citrate de Choline) La plupart des spécialistes eurent l occasion de prescrire ce médicament et ne partagèrent pas tous l enthousiasme des premiers utilisateurs Au reste n est il pas un peu déraisonnable d exiger d un médicament quel qu il soit la régénération d une cellule aussi hautement différenciée que la cellule auditive?

Par contre il nous a paru raisonnable de tester l action préventive possible de ce médicament et les résultats nous paraissent encourageants Sur les dix cochlées reconstruites dans le groupe KO (fig 6) six sont rigoureusement indemnes quatre présentent des lésions dégénératives beaucoup moins étendues que dans le groupe K C est dans le groupe KO seul que l on trouve des organes de Corti paraissant avoir échappé aux effets toxiques de l antibiotique (à une dose 20 fois supérieure à la dose thérapeutique humaine)

Il est possible que nous détenions avec l aminovitaminothérapie un procédé susceptible de réduire les accidents de surdité imputables à la Kanamycine et à la Dihydrostreptomycine notamment Il semble que des essais cliniques puissent être tentés dans ce sens

SUMMARY

The authors are wondering whether a preventive treatment could possibly reduce or prevent the inner ear from lesions caused by toxic antibiotics (Streptomycine, Dihydrostreptomycine and Kanamycine)

They experimented on guinea pigs already under Kanamycine treatment If the administration of corticoids shows itself a bit deceiving a solution composed of Vitamine B complex and amino acids is able to protect the organ of Corti 6 times out of 10 and to reduce the lesions 4 times out of 10 although the dose of Kanamycine used was 20 times bigger than the therapeutic dose

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DISCUSSION

E Surala When trying to avoid a damage of hearing in cases where a treatment with Kanamycine is unavoidable it is important to investigate and make sure that the renal function is undisturbed A good renal function is a conditio sine qua non without which a treatment with Kanamycine is not possible and contra indicated because of cumulation of the drug in the body Vitamins and amino acids may be good but a good renal function is inevitable

May I ask if the renal function of the test animals was investigated?

P Ardouin A Tours ou nous suivons régulierement les audiogrammes du centre de Phtisiologie, nous nous sommes penchés depuis deux ans sur la question de

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at an early stage and the importance of special treatment and training The latter should be initiated as soon as possible, preferably as early as the pre school age

3 The legal ordinances which assess aptitude in deaf car drivers are often different in different countries and are sometimes too restrictive This discrimination against the hard of hearing should be reduced or abolished The World Federation requests the authorities concerned to devote special attention to this question

Meyer zum Gottesberge Bei histochemischen Untersuchungen auf Aminosauren findet man mit verschiedenen Methoden eine auffallige Anreicherung in der Region der Innenpfeiler und des Kopfes der inneren Haarzellen Konnte bei den Schadigungen der Haarzellen ein Unterschied der inneren oder ausseren festgestellt werden?

P Pialoux Je voudrais souligner l'importance, à mon sens capitale, de ce qu'on peut appeler le facteur « susceptibilité individuelle » dans la pathogène des toxiques du labyrinthe — le facteur est indiscutable chez l'homme

Il est vraisemblable qu'il existe aussi chez l'animal — le facteur ne s'explique pas entièrement par un éventuel element rénal — les travaux du Pr M Portmann tendent à prouver qu'on ne peut pas non plus le mettre uniquement sur le compte de l'allergie

J J Groen I want to refer to a typical aspect of e g streptomycine poisoning in the delayed action

We all know of patients who only show the first symptoms after a few months resulting in a loss of say 60 db But then even after years one sees that a new loss has commenced This delayed action is rather frightening Is there any indication in your animal experiments which points to a delayed degenerative action of these toxic agents or their products which are left behind?

M Portmann (Reponse) Au Dr Sirala Il est exact que la perméabilité rénale joue un rôle tres important dans l'ototoxicité des antibiotiques Nous n'avons malheureusement pas fait d'epreuves rénales sur nos animaux que nous avons considérés a priori comme normaux à ce point de vue

Au Dr Ardouin Je remercie le Prof Ardouin pour son aimable intervention, ses travaux paraissent en effet confirmer les notres

Au Dr Holmgren Il parait en effet très important de faire connaître les dangers de certains antibiotiques et d'obtenir que les produits ototoxiques ne puissent être prescrits sans contrôle

Au Dr Meyer Les cellules ciliees internes sont en général intactes, les cellules ciliees externes seules lésées

Au Dr Pialoux Je suis tout a fait d'accord avec Mr Pilaoux sur le fait que le facteur rénal n'explique pas toutes les variations individuelles Il existe surement une fragilite personnelle de nature constitutionelle et génétique

Au Dr Groen On peut expliquer les surdités survenues a retardement avec délai apres le traitement toxique de plusieurs façons Les résultats de certains travaux de notre ecole publiés par les Dr Darrouzet et De Lima il y a un an (Revue de Laryng Supplementum Phono Audiologie Aout 1962) semblent donner une explication à ces surdités toxiques retardees Ces auteurs ont pris 4 groupes de Cobayes

le premier reçoit une certaine dose de Kanamycine
le second un traumatisme sonore minime
le troisième le même trauma sonore puis la meme dose de Kanamycine que le 1er
le quatrième la même dose de Kanamycine que le 1er puis la meme trauma sonore que le 2me

l'ototoxicité des antibiotiques majeurs, et, l'an dernier, au sein meme de cette Société, *nous avions présenté le résultat de nos recherches*

Mais il n'est pas douteux que le probleme essentiel est celui de la prévention des accidents thérapeutiques

On peut essayer de résoudre ce problème de deux façons ·

a) soit en diminuant la toxicité intrinsèque du produit,

b) soit en protégeant directement la cochlée par l'administration d une substance augmentant la résistance des cellules de Corti à l'agression médicamenteuse

Dans ce but, nous avons commencé, depuis bientôt un an, deux séries de tentatives en administrant, dans les deux cas, la substance protectrice en meme temps que l'antibiotique ·

a) d'une part, avec un complexe vitaminique B,

d) d'autre part, en utilisant un soluté d'acide adénosine 5 triphosphorique (exactement la Triphosadenine du codex), dont le rôle catalyseur dans les oxydations cellulaires est puissant et indéniable

Dans les deux séries d'experiences, nous avons opéré avec des doses très importantes, désirant provoquer une intoxication aiguè

En ce qui concerne les RÉSULTATS ·

1° Dans l'ensemble, nous n'avons pas obtenu de modifications sensibles avec la vitamine B

2° Tandis qu'avec la Triphosadénine, le lot de cobayes survivants a *été plus* élevé, et surtout les lésions fonctionnelles, vérifiees par les potentiels microphoniques et les *potentiels d'action, nous ont paru nettement diminuées*

Nous n'avons pas encore publié le résultat exact de nos recherches, car il nous a semblé qu'un nombre très important de sujets était nécessaire, étant donné l extrême variabilité individuelle des lésions histologiques et des réponses cochléaires, suivant les individus

La puissance ototoxique d un produit dépend, en effet, en grande partie, de la valeur de la barrière hémolabyrinthique responsable du degré de concentration et de la facilité du passage de l'antibiotique

Et là encore, on se heurte à de grandes inconnues dans la modalité de la régulation des échanges liquidiens endolabyrinthiques

Il n'en est pas moins vrai que seuls les résultats positifs comptent, et c est pourquoi j'ai été très intéressé par la très belle communication du Professeur Michel Portmann, et je tiens à le féliciter doublement d'etre parvenu à ces beaux résultats, surtout avec la concentration d'antibiotique utilisée, qui est une dose très supérieure à la dose léthale

L. Holmgren At the IV World Congress of the Deaf in Stockholm *August 1963*, the first of the main subjects was damages of the hearing organ caused by antibiotics The following resolution was accepted by the medical commission and the general assembly

1 The Commission on Medicine and Audiology in the World Federation of the Deaf, having discussed *deafness caused by streptomycin and other antibiotics*, wishes once more to emphasize the part which certain antibiotics and especially dihydrostreptomycin play as a cause of deafness Accordingly the Commission urges the medical organizations and governments of different countries, as well as international political and non-political organizations, to take all necessary steps to counteract this danger, *in the interests of public health*

2 The Commission stresses, on the other hand, the necessity of diagnosing deafness

ON SCLEROMA

A. Zakrzewski and A. Durska-Zakrzewska
Poznan, Poland

From the Oto-laryngological Clinic of the Medical Academy in Poznan

Conclusions were drawn from bacteriological, histological and serological studies on 164 patients clinically observed for 3-13 years. Full recovery from scleroma was obtained in 70% of cases.

Age of patients, duration of disease and manner of specific treatment were the decisive factors of curability. A hitherto unknown scheme of treating scleroma with streptomycin and other antibiotics was elaborated. This paper is the first exhaustive review of the scleroma curability problem.

Scleroma is a chronic specific disease of the upper parts of the respiratory tract. It is characterized by a slow development of hard infiltrations in the mucosae of nasal cavities, sometimes on the skin of the nose, in the mucosa of the nasopharynx, larynx, and even trachea and bronchi. The hard infiltrations do not ulcerate. They bring about a gradually increasing dyspnea which formerly necessitated tracheotomy. The disease is caused by the capsulated bacterium of the Klebsiella group, discovered by Frisch in 1882. Histological structure of the infiltration is very characteristic, mainly by the presence of large Mikulicz cells. Scleroma appears only in some regions of our globe, viz. on the western frontier of the Soviet Union and the eastern part of Poland, in Czechoslovakia, Middle America, North Africa and in the Far East. Nowadays, however, the scleroma patients can be found not only in the countries with endemic foci of the disease, but nearly in all countries of all continents. Not all cases of the disease are easily diagnosed in countries in which scleroma occurs very rarely. The atrophic form of the nose scleroma is often misdiagnosed as ozena, and the hypertrophic form of the larynx scleroma as non-specific laryngitis.

The migration of people after the Second World War and travelling facilities helped to spread the disease so that cases of scleroma can be found practically everywhere nowadays. This is what justifies this paper, presenting the results of laboratory and clinical investigations ...

... rmatologist from Vienna, almost a hundred years ago. The former name of the disease was rhinoscleroma, because Hebra as dermatologist at first knew only the skin forms of scleroma.

By the time the streptomycin was discovered, there had been no specific treatment. Vaccines, X-ray therapy and various surgical procedures, above all dilatations of narrowed larynx and trachea, were applied.

Les résultats ont montré que le traumatisme sonore ne paraît pas fragiliser l'oreille vis à vis du toxique mais par contre le toxique (Kanamycine) fragilise l'oreille vis à vis du traumatisme sonore.

Ainsi un oreille même normale en apparence peut avoir été fragilisée par le traitement ototoxique La surdité ne se révélera qu'ultérieurement à l'occasion de l action d'un autre facteur étiologique Cette notion paraît primordiale pour les examens otologiques des travailleurs employés à des travaux bruyants Elle constitue une des explications possibles du délai parfois rencontré en clinique humaine

in vitro as the time went by did not demonstrate their previously acquired resistance to streptomycin

Those experiments have brought us to the conclusion that as the treatment goes on the therapeutic doses cannot remain on the same level throughout the treatment but they must be on the increase Taking into consideration the first clinical cases of scleroma treated with streptomycin and mostly requiring ca 120 g of streptomycin as well as the experiments presented above we suggest the following schedule of dosing streptomycin 0 5 g of streptomycin daily for the first 40 days 1 0 g daily for another 60 days 2 0 g daily for the rest of the time until the treatment is finished

This kind of therapy has been applied to 164 cases of scleroma since 1949 To calculate the results in per cent we selected only the cases in which the control period after the termination of treatment was not less than three years a period long enough to assess the effectiveness of treatment In order to evaluate the efficacity of the drug properly and check the rightness of dosing we took only the cases in which all criteria of curability were considered i e the clinical condition and results of bacteriological serological and histopathological examinations

Below are listed the total doses of streptomycin administered in different groups of patients

20–100 g SM in 23 cases	101 200 g SM in 68 cases (including 39 cases 101 150 g SM)
201 300 g SM in 47 cases (including 27 cases 201 250 g SM)	301 400 g SM in 10 cases

Maximum dose 450 g SM 1 case

Thus out of the total of 152 scleroma patients treated with streptomycin 118 patients were given up to 250 0 g and only 31 patients a total of over 250 0 g The three last patients were not added as they are still under treatment

As the therapy was as a rule followed without interruptions and all the other methods nowadays already historical ones were discarded our material must be regarded as uniform and large enough to allow the conclusion to be drawn that the data obtained from the experiments in vitro made it possible to elaborate practically the right schedule for dosing streptomycin in scleroma We are of the opinion that high doses of streptomycin given to patients under treatment did not bring about any serious complications to the VIII nerve Out of 152 patients treated with streptomycin only one female patient attributed her hard hearing to the drug The anamnesis before the start of her treatment showed that her complaints of hard hearing dated back many years before her disease was diagnosed Thus even in

Gordon New and collaborators from the Mayo Clinic were the first to employ streptomycin in 1948 which proved to be the specific medicine That date is to be regarded as the turning point in the history of scleroma as much as the year 1870 when Hebra established the disease as an entity and the year 1882 when Frisch discovered capsulated bacteria As the knowledge of properties of antibiotics was developing and the phenomenon of the bacteria becoming resistant to antibiotics was found the necessity arose of examining the capsulated bacterium of scleroma in this respect all the more so as it was well known that the whole dose to cure the disease would be high at least 100 g There was fear of recurrence of the chronic disease if always the same unchanged daily doses were administered in the course of a long cure especially in face of the fact that streptomycin in contrast to penicillin and other antibiotics brings about very readily the resistance to streptomycin of the treated microbes The possibility had to be taken into account of developing resistant strains that might infect healthy people living with scleroma patients which would be most undesirable from the epidemiological point of view Starting our work on the resistance of scleroma capsulated bacterium to streptomycin we had no data from literature to refer to and had to follow to some extent on the lines of investigations made on the bacillus of tuberculosis

The investigations *in vitro* on sensitivity of scleroma capsulated bacterium to streptomycin were carried out on liquid broth media the lowest streptomycin concentrations being 0 1 mcg/1 ml liquid medium and the highest amounting to 100 mcg/1 ml unattainable in the blood serum of the treated patients

The growth of Frisch capsulated bacteria taken from sick persons not yet treated was inhibited at streptomycin concentrations as low as 0 1 0 25 and 0 5 mcg/1 ml broth medium The Frisch capsulated bacterium is among the microbes extremely sensitive to the inhibitory action of streptomycin The sensitivity of Frisch bacillus to other antibiotics was uncomparably smaller Penicillin and aureomycin induced the growth inhibition of all studied strains of Frisch bacillus only at the concentration as high as 100 mcg/1 ml broth medium and chloromycetin at 1 to 5 mcg/1 ml Besides streptomycin the terramycin may be taken into account as a drug practically effective in treating scleroma In order to investigate the phenomenon of the microbe acquiring resistance to streptomycin various strains of Frisch capsulated bacteria were bred in a liquid medium at subthreshold streptomycin concentrations It was found that the microbes became resistant to streptomycin very readily and the concentration even 500 times higher could not manage to inhibit the growth of some strains

The microbes which became resistant *in vitro* did not lose their resistance when transplanted on the liquid medium without subthreshold doses of streptomycin whereas the strains isolated from mucous membrane of patients with recurrences previously treated with streptomycin that is to say the strains which as we found had become resistant 3 5 and 20 times

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The investigations *in vitro* on sensitivity of scleroma capsulated bacterium to streptomycin were carried out on liquid broth media, the lowest streptomycin concentrations being 0.1 mcg/1 ml liquid medium and *the highest* amounting to 100 mcg/1 ml, unattainable in the blood serum of the treated patients.

The growth of Frisch capsulated bacteria taken from sick persons not yet treated was inhibited at streptomycin concentrations as low as 0.1, 0.25 and 0.5 mcg/1 ml broth medium. The Frisch capsulated *bacterium* is among the microbes extremely sensitive to the inhibitory action of streptomycin. The sensitivity of Frisch bacillus to other antibiotics was incomparably smaller. *Penicillin and aureomycin induced the growth inhibition* of all studied strains of Frisch bacillus only at the concentration as high as 100 mcg/1 ml broth medium and chloromycetin at 1 to 5 mcg/1 ml. Besides streptomycin the terramycin may be taken into account as a drug practically effective in treating scleroma. In order to investigate the phenomenon of *the microbe acquiring resistance* to streptomycin various strains of Frisch capsulated bacteria were bred in a liquid medium at subthreshold streptomycin concentrations. It was found that *the microbes became resistant to* streptomycin very readily and the concentration even 500 times higher could not manage to inhibit the growth of some strains.

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examined before starting therapy in order to facilitate the choice of the most efficacious antibiotic and establish the daily dose of the drug

4 The therapy should be carried out without interruptions with gradually increasing daily doses until full clinical recovery is obtained confirmed by negative results of bacteriological serological and histological examinations

5 X ray therapy, dilatation methods and all other measures formerly employed ought to be discarded as superfluous and even harmful ones as they make full restitution *ad intergrum* difficult

RÉSUMÉ

Les conclusions obtenues après 3 13 ans d observation clinique et d examens bactériologiques histologiques et sérologiques ont été basées sur un matériel de 161 malades Tenant compte de tous les critères de guérison on a noté une guérison complète dans 70 % des cas

Dans le guérison le facteur décisif est l âge du malade la durée de la maladie et la méthode de traitement spécifique On a élaboré un schéma non existant jusqu ici de traitement du sclérome par la streptomycine et les autres antibiotiques Le travail passe pour la première fois en revue les divers aspects du *problème de la curabilité* du sclérome

ZUSAMMENFASSUNG

Unsere Schlussfolgerungen zu welchen wir nach einer 3 13jährigen klinischen Beobachtung sowie auf Grund von bakteriologischen histopathologischen und serologischen Untersuchungen gekommen sind liegt ein Erfahrungsgut von 161 Kranken zugrunde Eine vollständige Heilung unter Berücksichtigung aller Kriterien erhielten wir in 70 % der Fälle

Die wichtigsten Faktoren im Heilungsprozess stellten das Alter der Kranken die Krankheitsdauer und die Art der Therapie dar Es wurde ein bisher nicht vorhandenes Schema für die Therapie des Skleroms mit Streptomycine und anderen Antibiotika ausgearbeitet Die Arbeit gibt zum ersten Mal einen ausführlichen Überblick über das Heilbarkeitsproblem des Skleroms

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... (In Polish with Eng ... ary)

1951 On dosage of streptomycin in scleroma *Otolaryngolog ...* with ...

195 ...

myt ...

this one case out of so many under treatment, the hard hearing could not be connected with streptomycin therapy.

The complications in the vestibular nerve used to be much more serious (Szmeja). As a rule, in all the patients after the application of 60 to 80 g of streptomycin, we found the deterioration of the vestibular function, examined by the caloric test. The caloric test control examination, made in 93 patients a number of years after the therapy was terminated, showed the recovery of caloric excitability in 85 per cent of cases. Out of 144 patients treated with streptomycin we recorded 101 recoveries with at least 3-year follow up period, confirmed by all criteria of curability, which constitutes 70.1 per cent. In further 20 cases of recovery we did not succeed to make control examinations. A few years after recovery the patients did not come to control examinations, although they were summoned to, or the addressees could not be found. In five cases the therapy was interrupted. In four patients a rather high resistance to antibiotics was found and in spite of large doses of antibiotics applied a complete recovery could not be obtained. In 14 cases under treatment we could observe a recurrence of disease. A part of them was cured after additional therapy.

Scrutinizing the cases of relapse it should be pointed out that the first signs of recurring disease were most frequently observed in serological reactions, many a time two or even more years earlier than the bacteriological, histological or clinical recurrences. Hence the great importance of that reaction as one of the objective tests of improvement in the course of treatment and in the follow up period of the patients many years after the therapy was ended. We observed the usefulness of terramycin in the therapy of scleroma. We employed it as the only antibiotic in 12 cases of the disease. A complete recovery with a long follow-up period was obtained in five cases, two further cured patients did not come to the control examination, in four cases recurrence was found, and one patient did not finish his therapy. Moreover, the terramycin was employed as a supplementary treatment in 18 patients treated with streptomycin.

The attempt to cure the scleroma patients with chloromycetin did not succeed, the total dose of 19 to 41 g given to five patients resulted in a slight improvement only at the time of administering the drug. When the treatment was stopped, however, a quick recurrence of the disease could be observed. This is why all further attempts to apply the drug were given up.

The results obtained by us in the therapy of scleroma patients prove that the schedule of dosing antibiotics and the methods of treatment are the right ones.

CONCLUSIONS

1. Scleroma has become a curable disease owing to antibiotics.
2. Streptomycin is a specific drug in scleroma. The average dose in our patients did not exceed 200.0 g SM.
3. In every case of scleroma the resistance of Frisch bacillus should be

La première a comme sujet la localisation du sclérome J'ai eu l'occasion d'en observer quelques cas venant de la côte occidentale d'Afrique

Parmi eux nous avons trouvé autrefois un sclérome seulement localisé à l arbre bronchique d un seul poumon, le nez et le larynx ainsi que la trachée étant nos maux, le prof Zakrzewski en a t il observé des cas?

La deuxième question est le sclérome est il en diminution en Europe? En *Afrique* ou je suis retourné recemment, il me semble que les cas sont beaucoup moins nombreux et suivent en cela la diminution de la lèpre sous l influence des thérapeutiques modernes

A Zakrzewski (Reply) I thank very much Prof Laskiewicz for his interesting remarks on the history of scleroma in Poland

A Portmann Pour répondre au prof Portmann je dois remarquer que les cas isolés de sclerome pulmonaire sans infiltration du nez et du larynx sont rares dans notre climat, mais ils sont rencontrés en Afrique et en Amérique Centrale En ce qui concerne la lèpre je ne connais pas bien ce problème Comparant la lèpre et le sclérome au point de vue de la fréquence on peut dire que le sclérome est rare, quelques milliers dans le monde, et quelque millions de lepreux

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The Otolaryngological Clinic
Medical Academy Poznan Poland
49 Przybyszewski street

DISCUSSION

A Laskiewicz Discussing the problem of treatment of scleroma of the upper and lower respiratory organs I would like to mention this Przemyslaw Pieniązek as a reader of Otolaryngology at the Jagiell Univers of Kraków in 1879 started to lecture on laryngology 84 years ago His name is associated with the low tracheoscopy in order to remove scleromatic infiltrations, which he had first performed in 1884 This picture shows a suffocating child with tracheostomy performed some weeks ago when removal of the tracheostomy tube did not improve his condition Pieniązek inserted one elongated aural speculum into the tracheostomy and the child s head was pushed back and slightly rotated in order to get the optimum position to throw down the reflected light from the ordinary oil lamp Then he removed with cutting forceps the floating masses of granulations from the deeper parts of tracheostoma, thereafter the respiration of the child become normal Pushing deeper this aural speculum he was able to see the whole trachea, the carina and even the bronchial lumina Soon after Pieniązek constructed one set of tracheal tubes for children and adults and some dilatating tubes of two halves During the pioneer period of his work a great number of scleroma of the upper and lower respiratory organs gave the most opportunities to apply the named tracheo bronchoscopy infer The first description of this type of endoscopy was published in his textbook of laryngology in 1887 In 1889 Pieniązek reported his tracheo bronchoscopic observations in the *Wr Medical Bulletin* Nos 44–45 In 1894 he presented one paper at the Congress of Naturalists and Physicians in Vienna about the surgical treatment of scleroma of the lower respiratory organs and seven cases of foreign bodies removed from the tracheo bronchial tree using the tracheo bronchoscopia inferior One year later Kirstein introduced his direct laryngo tracheoscopy, and in 1898 Killian succeeded in his peroral direct tracheo bronchoscopy

G Portmann Le prof Zakrzewski a une très grande expérience du sclérome — aussi me permettrai — je de lui poser deux questions



Fig 1 Labyrinthitis Pigmented macrophages within the connective tissue of the planum semilunatum

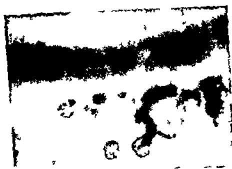


Fig 2 Labyrinthitis Pigmented macrophages as adventitial cells

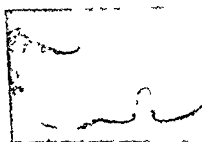


Fig 3 Labyrinthine hemorrhage Pigment in the planum semilunatum and in the canalicular wall

of the perilymphatic spaces of the semicircular canals and of the utricule are rich in pigment which is contained *in the* polymorphous cells In the planum semilunatum the dyed *cells are* globose or oval and so *filled up* with pigment that the nucleus is hardly noticeable (Fig 1) while in the semicircular canals they are star or *spindle shaped leaning against* and sometimes wrapping the smaller vessels (*Fig 2*) *These cells can be seen to* contain few granules of pigment

In the labyrinthine hemorrhage *in guinea pigs* the dyed cells widely infiltrate the planum (Fig 3) the wall *of the utricle and constitute a net*

NATURE OF A PIGMENTED SUBSTANCE IN THE LABYRINTH

E. Borghesan
Palermo, Italy

From the Oto-laryngological Clinic of the University of Palermo

The pigment existing in the loose connective tissue of the posterior labyrinth is originated by hemorrhage, pathological or physiological inflammations and wearing out of tissues. Such pigment is contained in macrophages.

In a previous paper I noticed that quite often a finely granulous dark grey osmio-reducing substance is contained in the epithelial cells among the cells themselves and in the interstitial spaces of the connective tissue of the planum semilunatum; the present researches concern another substance constituted of small dark brown refracting granules contained in the polymorphous cells of the loose connective tissue of the posterior labyrinth.

Catalano & Madonia (1963) have recently published the results of researches concerning a brown pigment found at the sides of the crista ampullaris and have considered it as an elaborate by specific cells: the melanocytes. These authors attribute a special function to such pigment, even if this function is not yet known, and think that the variable quantity of the pigment is related to chemical modifications taking place in the tissues because of cadaveric alterations. I am not aware of other studies on this argument.

For some years I have been gathering a histological documentation in order to explain the significance of the pigmented substance existing in the planum semilunatum; today I think I have elements enough to afford an interpretation. The histological researches concern two labyrinths of human foetus, several of rabbits and guinea pigs, either normal (as normal I considered the labyrinths which had undergone no experiments) or under experimental conditions.

All the labyrinths have been fixed *post mortem*; those of human foetus and of rabbits in osmic acid and iron hematoxylin stained; those of guinea pigs have been treated with Marchi's method and with no contrast staining.

In the labyrinths of human foetus, of rabbits and normal guinea pigs the pigmented substance is found almost always, though in little quantity, but it may be lacking even in the labyrinths fixed too late. The pigment accumulates in the loose connective tissue, especially of the planum semilunatum, and is intracellular.

In the experimental labyrinthitis the loose connective tissue of the planum

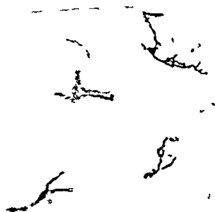


Fig 6 Pigmented macrophages as clasmatocytes



Fi Hemorrhagic focus with pigmented macrophages as clasmatocytes surrounding a glomerular art r of the co lea

tilial cells They all are able to ingest many types of particular matter and to store s me of them electively working as histogenous macrophages on account of the inflammation many of them turn into free macrophages

The pigment found in the cells seems as to quality the same its origin, however is different because that contained in the histiocytes of a hemorrhagic focus is very likely hemosiderin deriving from the hemoglobin of the erythrocytes in decomposition whereas the pigment found in the labyrinthus is a melanin deriving from the protides Consequently, the pigmented cells are not melanocytes in which melanin is autogenous but are macrophages constituting a system that (owing to accidental events) assumes the occasional aspect of chromatophores



FIG. 4. Labyrinthine hemorrhage. Macrophages constituting a pericanalicular net.



FIG. 5. Macrophages of preceding fig. [illegible] One of these macrophages surrounds a capillary.

around the semicircular canals (Fig. 4). Such net is run over by vessels whose walls are dotted with black dye and is constituted of large cells with branched processes and a clear nucleus delimited by a membrane on which rest very small black granules (Fig. 5). Other cells with globose nucleus and spindle shaped protoplasm are scattered in the pericanalicular loose connective tissue (Fig. 6) and can be found also round the glomerular arteries of the cochlea (Fig. 7) of the ampullae and around the big vessels of the stria vascularis when these are within hemorrhagic focus (Fig. 8).

The pigment has never been found in the endolymphatic spaces and in the perilymphatic ones deprived of loose connective tissue.

In almost all of the labyrinths examined the brown pigment is present but it appears in greater quantity and is more widely spread in the pathological labyrinths; this pigment is traceable only in the zones provided with loose connective tissue and is almost always intracellular. The pigmented cells are polymorphous histiocytes, clasmatocytes, rhagiocrine cells, adven-

DISCUSSION

G Portmann J ai été très intéressé par le travail du M Borghesan Il y a de nombreuses années alors que je faisais systématiquement des coups histologiques de l oreille interne, j ai eu l occasion de constater la présence de pigment dans le labyrinthe antérieur au niveau de la columelle

Je me suis demandé alors si les fonctions sensorielles n'exigeaient pas la présence de pigments — car nous avons déjà la tâche presente « locus lectuers » pour le nerf alfacht et la couche pigmentaire de la retion pour le nerf optique

M Borghesan a t il fait des constatations analogues? En tous cas je le felicite de son travail et pense qu un tel sujet mérite de nouvelles recherches

E Borghesan (Réponse) Dans les espaces endolymphatiques du *labyrinthe et dans* ceux des prélymphatiques de la cochlée, je n ai pas vu de cellules pigmentées Ces cellules sont toujours là ou il y a du tissu conjonctif lâche



Fig 8 Pigmented macrophages and fragments of erythrocytes surrounding a big vessel of the stria vascularis

This system, a true potential defensive device and the almost constant presence of pigmented macrophages in normal semicircular canals induce us to think that in the perilymphatic spaces, even in physiological conditions may exist endogenous substances deriving from embryonal or worn out tissues that stimulate the activity of the macrophages giving origin to a histological reaction that Bloom & Fawcett have called physiological inflammation It is besides suggested that this eventuality in the semicircular canals may be provoked by small and not exceptional causes for instance by very little hemorrhages either spontaneous or traumatic, for which the posterior labyrinth seems to have an anatomical predisposition long thin and fragile blood vessels

RÉSUMÉ

Le pigment existant dans le tissu conjonctif lâche du labyrinthe postérieur est causé par hémorragie inflammation pathologique ou physiologique ou par l usure des tissus Ce pigment est contenu dans des macrophages

ZUSAMMENFASSUNG

Das Pigment, dass sich im losen Bindegewebe des Labyrinths befindet, entsteht vielleicht durch Bluterguss Entzundung „physiologische Entzundung oder auch normale Gewebeabnutzung Dieses Pigment ist regelmässig in Makrophagen enthalten

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sur le canal semicirculaire externe gauche Toutes les experiences furent controlees au moyen de l introduction dans l endolymphe du solvant de chacune des substances employees Les resultats negatifs obtenus nous permettent d affirmer que les divers phenomenes observes dans nos series d expériences sont dus exclusivement à l action de ces substances

Experiences avec chlorure d acetylcholine diisopropilfluorophosphate solphate d atropine

L ouverture des deux fistules dans le canal semicirculaire lateral provoque une reduction de la reflectivite de ce canal semicirculaire a l epreuve rotatoire Cette reduction de reflectivite est accompagnee par une reduction égale de la reflectivite du canal semicirculaire externe contrelateral

L introduction dans l endolymphe de chacune des substances provoque apres un bref interval de temps l apparition d un nystagme horizontal rotatoire dont la phase rapide se dirige dans le sens contrelateral au labyrinthe opere Ce phenomene presente selon les cas une duree de 1 et 1

Les controles electronystagmographiques avec epreuve rotatoire executes apres 15 et 90 de la fin de ce phenomene demontrent l existence d une reflectivite presque symetrique des deux canaux semicirculaires lateraux reflectivite qui est a peu pres egale a celle que l on retrouvait avant de commencer l experience

Experiences avec chlorure de tetra ethylammonium

L introduction dans l endolymphe de tetra ethylammonium n a jamais determine l apparition d un nystagme horizontal rotatoire Les controles electronystagmographiques au moyen de l epreuve rotatoire effectues apres 15 et 90 de l introduction de tetra ethylammonium n ont pas demontr l existenc [illegible]
lateraux

L inte [illegible] obtenus dans ces recherches est difficile a cause des motifs suivants

a) on ne peut etablir exactement la quantite de chacune des substances employees qui agit sur le neuroepithelium

b) certaines de ces substances en relation a leur concentration peuvent produire un effet oppose

c) on ne peut exclure que certaines de ces substances agissent dans ces experiences non seulement dans les phenomenes de transmission des impulsions nerveuses mais aussi avec un mecanisme pharmacodynamique direct

Tout en tenant compte de ces reserves il est logique de presumer que dans les experiences effectuees avec l acetylcholine on determine une accumulation de cette substance dans tout le complexe constitue par le recepteur la fibre afferente et celle efferente

A l accumulation de cette substance correspond du point de vue fonctionnel l apparition d un nistagmus horizontal rotatoire dont la phase rapide se

L'ACTION LOCALE DE L'ACÉTYLCHOLINE, DE SUBSTANCES ANTICHOLINERGIQUES ET ANTICHOLINESTÉRASIQUES SUR LA FONCTION VESTIBULAIRE

Recherches expérimentales

F. Brunetti, G. Rossi, G. Voena, S. Buongiovanni et G. Cortesina
Turin et Sassari, Italie

Clinique Otorhinolaryngologique de l'Université de Turin (Directeur: Prof. F. Brunetti) et Institut d'Anatomie humaine normale de l'Université de Sassari (Directeur: Prof. G. Filogamo)

On a étudié sur le lapin les effets dûs à l'action directe de l'acétylcholine, du diisopropylfluorophosphate, du tetraethylammonium et de l'atropine sur la fonction des récepteurs vestibulaires.

Sur la base des résultats ainsi obtenus, on peut arriver à déduire que l'acétylcholine prend part tant au processus de transmission des stimuli nerveux du récepteur ampullaire à la fibre efférente qu'au mécanisme qui règle la transmission quantitative de ces stimuli.

Nous avons récemment étudié les effets produits sur la fonction vestibulaire par l'introduction d'acétylcholine, de composés anticholinergiques et de substances anticholinestérasiques dans l'endolymphe, puisque des recherches anatomiques, histochimiques et expérimentales récentes font supposer l'existence, au niveau du complexe formé par le récepteur vestibulaire, la fibre afférente et celle efférente, d'un mécanisme de transmission chimique de l'impulsion nerveuse sur la base du système acétylcholine, cholinacétylase, acétylcholinestérase, en relation avec les fibres vestibulaires efférentes (Petroff, Wersäll, Smith, Rasmussen & Gacek, Dohlman, Farkashidy & Salonna, Engström, Carpenter, Bard & Alling, Carpenter, Gacek, Ireland & Farkashidy, Rossi, Rossi & Cortesina, Sala, Schmidt).

Nos recherches ont été effectuées sur 82 lapins (Lepus cuniculus L.), animal qui d'après les recherches de Rossi et Cortesina possède les mêmes structures anatomiques efférentes observées par les mêmes auteurs chez le cobaye.

La pénétration dans l'endolymphe des substances examinées a été obtenue avec le système de la double fistolisation du canal semicirculaire latéral et a été controlée histologiquement par une série d'expériences préliminaires au moyen de l'addition d'un colorant vital (bleu de méthylène).

L'étude fonctionnelle des substances examinées a été faite au moyen de la registration électronystagmographique. Ces expériences ont été effectuées

physiologiques l'acetylcholine prend part au niveau du neuroépithelium des crêtes ampullaires au mécanisme qui détermine et règle la transmission des impulsions afférentes

SUMMARY

We have studied experimentally the effects of the direct action of acetylcholine, diisopropylfluorinphosphate, tetraethylammonium and atropine upon the function of vestibular receptors in rabbits

From the results of this research it seems that acetylcholine contributes both to the transmission of the nerve impulses of the ampullar receptors to the efferent fibers and to the mechanism which regulates the extent of the transmission of these impulses

ZUSAMMENFASSUNG

Es wurden in Kaninchen die Ergebnisse der direkten Wirkung von Acetylcholin Diisopropylfluorophosphat Tetraatylammonium und Atropin auf die Funktion der vestibularen Rezeptoren experimentell untersucht

Aus den obengenannten Untersuchungen ergibt sich scheinbar, dass Acetylcholin am Überführungsprozess der nervösen Reizungen vom ampullaren Rezeptor zu den efferenten Fasern und am Regulierungsmechanismus der quantitativen Reizüberführung teilnimmt

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dirige dans la direction du labyrinthe contrelatéral à celui où on a provoqué l'accumulation d'acétylcholine.

Ce phénomène pourrait être mis en relation avec la réduction ou l'abolition unilatérale des impulsions que même à l'état de repos les crêtes ampullaires envoient aux centres, impulsions dont l'existence a déjà été démontrée avec la méthode électrophysiologique par Lowenstein et Sand, Gernandt, Ledoux.

Les expériences effectuées avec l'acétylcholine ne permettent pas de préciser le siège et la nature de ce processus d'inhibition de la transmission des impulsions afférentes.

Dans les expériences faites avec le diisopropilfluorophosphate on provoque une *accumulation d'acétylcholine limitée théoriquement* à la synapsis entre fibre efférente et système constitué par le récepteur et la fibre afférente.

L'*effet fonctionnel constaté serait, dans ce cas, aussi la conséquence* de la réduction et de l'abolition unilatérale des impulsions afférentes qui se produirait avec les mêmes modalités déjà mentionnées.

La singulière richesse en acétylcholinestérase des boutons terminaux des fibres efférentes et les caractéristiques des rapports synaptiques qu'il contractent avec le système formé par le récepteur et la *fibre afférente* fait penser que l'inhibition de la transmission des impulsions afférentes soit la *conséquence de l'accumulation d'acétylcholine qui,* dans ces expériences, se vérifierait seulement au niveau des boutons synaptiques efférents et qui agirait sur des structures anatomiques non parfaitement identifiables mais qui font sûrement partie du système formé par le récepteur et la fibre afférente.

Le siège particulier dans lequel semble être circonscrit l'accumulation d'acétylcholine fait penser que, dans des conditions physiologiques, les *fibres efférentes libèrent l'acétylcholine* à ce même niveau.

Dans les expériences effectuées avec le tétraéthylammonium et l'atropine on a tenté de vérifier dans quel siège se trouve l'acétylcholine dans les conditions physiologiques en déterminant le bloc des effets produits par cette substance.

Le tétraéthylammonium n'a jamais provoqué l'apparition d'aucun effet fonctionnel. Dans les expériences effectuées avec l'atropine, on a observé *l'apparition d'un effet fonctionnel qui est, dans ce cas, aussi la conséquence* de la réduction ou de l'abolition unilatérale des impulsions afférentes.

Les résultats des expériences avec l'atropine et l'apparente antithèse constituée par les effets fonctionnels identiques obtenus dans ces expériences et celles où l'on détermine l'accumulation d'acétylcholine sembleraient démontrer que l'acétylcholine fait partie du mécanisme de transmission de l'impulsion nerveuse du récepteur à la fibre afférente.

En effet, si l'*acétylcholine* exerçait son action exclusivement au niveau de la synapsis entre la fibre efférente et le système formé par le récepteur et la fibre afférente, les effets fonctionnels observés ne devraient pas exister parceque l'atropine déterminerait seulement le bloc des impulsions efférentes.

Il nous semble par conséquent possible d'affirmer que dans les conditions

ÉTUDE DES VARIATIONS DE PRESSION DES LIQUIDES LABYRINTHIQUES[1]

M. Aubry, P. Pialoux et M. Burgeat
Paris, France

Une technique d'enregistrement de la pression des liquides labyrinthiques a été mise au point. Les modifications de la pression labyrinthique ont été étudiées au cours de plusieurs types de stimulation: variations de la pression aérienne extérieure et exposition à des sons purs très intenses.

Il a été constaté des modifications de la pression des liquides labyrinthiques sous l'influence de ces stimulations dont l'origine peut être, soit mécanique, soit biologique.

Il est permis de penser que les mouvements liquidiens imprimés par la platine de l'étrier peuvent se transmettre suivant certaines conditions à une portion ou à la totalité du labyrinthe. Ces mouvements liquidiens *provoquent* des variations de pression.

Il nous a paru intéressant:

- de souligner d'une part que les variations de pression endolabyrinthique pouvaient être déclenchées non seulement par action directe, mais aussi par l'émission de sons intenses;
- de souligner d'autre part le rôle joué par le système de transmission de l'oreille moyenne au cours de ces variations.

MÉTHODES D'ÉTUDES

Nous avons utilisé pour cette étude des *Mériones Crassus*. Ces animaux ont pour intéressante particularité d'être dotés de bulles tympaniques très volumineuses dont l'ouverture donne très aisément accès à l'ensemble du labyrinthe.

Après anesthésie de l'animal au Dial, on sectionne le conduit auditif et on ouvre largement la bulle tympanique. L'animal est ensuite placé sur une table de stéréotaxie de Horsley-Clarke dont les pointes d'oreilles creuses sont adaptées au conduit auditif externe et cimentées. L'absence de fuite est contrôlée au manomètre.

Selon une technique qui nous permet d'obtenir une étanchéité complète nous mettons en place des sondes de mesure de 6/10 de mm dans les différents points du labyrinthe que nous désirons tester. Ces sondes, remplies de sérum, sont reliées au capteur d'un manomètre électronique Telco dont

[1] Ce travail a été fait grâce à l'appui financier de la Direction des Recherches et Moyens d'Essais de la Défense Nationale.

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Clinique Otorhinolaryngologique de l Université de Turin Italie

DISCUSSION

H Engstrom During the last decade a revolution has taken place in our knowledge of afferent and efferent innervation In many sensory organs the amount of efferent nerve endings has been amazingly high and studies by Eccles and collaborators and many other have clearly shown the physiological importance of these feed back systems Cortesina and Rossi have made important contributions to the knowledge of efferent innervation of the inner ear It has been a most interesting opportunity to hear how these studies have now begun to be fitted into their clinical position and I want to congratulate Prof Brunetti and collaborators on an extremely interesting presentation I am personally convinced that one of the most important problems in the understanding of the physiology of the labyrinth is to elucidate the structure and physiology of the neural interconnections

M Arslan Brunetti and his coworkers demonstrated in 1962 the first hystochemical observation of the efferent fibers of the vestibular apparatus

From another point of view, Sala, in the ENT Dept of Padua, has demonstrated the electrophysiological activity of vestibular fibers after excitation of the contralateral vestibular efferent central fibers (*Experientia*, Vol 19, p 39, 1963)

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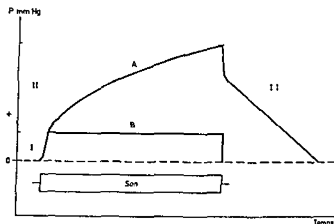


Fig. 1. Les résultats de l'expérience. A: Courbe obtenue chez l'animal vivant. B: Courbe obtenue chez l'animal mort. I: Montée brusque mais faible liée au phénomène physique. II: Montée lente mais importante liée au phénomène biologique. III: Chute de la courbe à la fin de l'émission sonore se faisant en deux temps: courte et rapide puis lente et prolongée.

la sensibilité nous permet d'enregistrer avec précision des variations de pression de 1/10 de mm de Hg dans les liquides labyrinthiques.

La lecture des variations de pression est faite sur un oscilloscope Tektronix 532 (déplacement du spot de 62 mm pour une variation de pression de 1 mm de mercure) dont la trace est photographiée.

Les variations de pression sont obtenues de deux façons:

— *soit à l'aide de sons.* Ceux-ci sont émis par un générateur de fréquences Philips 2308 permettant d'obtenir des intensités de 135 décibels re $2 \cdot 10^{-4}$ ba pour certaines fréquences de résonnance dans le circuit haut-parleur—pointe creuse.

— *soit à l'aide de variations de pression aérienne mécanique.* Celles-ci sont produites à l'aide d'une seringue entraînant une pression uniforme positive ou négative jusqu'à + ou − 12 mm Hg.

— *ou à l'aide d'une pompe de Palmer* permettant d'obtenir une pression alternative qui entraîne la production d'infra-sons de 123 db à la fréquence de 3 Hz.

Dans ce cas, un manomètre à eau est intercalé en série dans le circuit de stimulation dans le double but:

— de filtrer les bruits liés au fonctionnement de la pompe de Palmer;
— et de contrôler l'amplitude des déplacements de volume et par là le contrôle des infra-sons. Ceux-ci sont mesurés avant l'expérience par un infra-sonomètre de Pimonof.

STIMULATION SONORE

A. *Deux types d'expérience sont pratiqués.*

1) Tout d'abord une vérification acoustique. Le capteur du manomètre est branché directement sur le haut-parleur. On constate pour les sons les plus intenses (Max. 156 db re $2 \cdot 10^{-4}$ ba) des variations de pression + maximum de 17/100 mm de Hg.

Ces pressions acoustiques sont donc très faibles comparées à celles enregistrées dans le labyrinthe, et nous semblent être d'une valeur très proche de ce que l'on appelle en acoustique physique une *Pression de Radiation*.

2) Ensuite le labyrinthe est interposé entre la pointe creuse et le manomètre. Dans les mêmes conditions, nous avons fait les constatations suivantes :

1° *La sonde du manomètre est placée dans l'utricule*

a) La pression se situe généralement entre 2 et 3 mm de mercure et a pu atteindre pour 700 Hz à 136 db : 3 mm 38 Hg. Cette variation est dans certaines limites proportionnelle à l'intensité du son émis.

b) Le spot oscilloscopique se situe au dessus de la ligne iso électrique de référence en surpression (parfois au dessous, impliquant une dépression).

Il existe donc, avec des émissions sonores très intenses, une nette et importante variation de la pression labyrinthique.

2° *La sonde placée dans un canal semi circulaire*

Les variations de pression sont beaucoup plus faibles que précédemment. Elles sont de l'ordre de quelques centièmes de mm de Hg.

Pour déterminer s'il existe néanmoins des mouvements de liquide dans les canaux, nous avons réalisé des enregistrements de déplacement de niveau liquide dans deux sondes capillaires placées simultanément en deux points d'un canal. Les variations de niveau étant lues directement à la loupe binoculaire.

Dans ces conditions, lorsqu'une sonde est en contact avec l'extrémité postérieure d'un canal, et l'autre sonde avec l'ampoule, nous avons pu constater dans certains cas des variations de pression de sens opposé entre les deux sondes. Ceci impliquerait l'existence de pressions différentes pouvant être à l'origine de courant à l'intérieur du canal. Par contre, si les deux sondes sont dans l'arc du canal, les variations de pression (+ ou −) nous ont paru se faire dans le même sens.

3° *Les expériences ont été également conduites*

a) Sur l'animal curarisé. Il est alors placé en respiration artificielle.

b) En modifiant le circuit hydraulique, c'est à dire en créant des fuites ou en obturant la fenêtre ronde.

c) Après destruction de l'appareil de transmission.

d) En faisant varier l'intensité et la fréquence.

Sur l'animal curarisé les irrégularités de la réponse disparaissent, l'amplitude de la déviation peut augmenter et le plateau devient stable. Il semble donc que les muscles de l'oreille moyenne ne soient pas responsables de ces variations de pression.

La présence de fuites peut être à l'origine de variations de pression négative.

— La rupture de l'appareil de transmission supprime l'apparition des [illegible] tâtes

B. *Interprétation*

L'étude détaillée du tracé permet de constater :

— une légère variation de pression survenant immédiatement à l'émission du son, de l'ordre de quelques centièmes de mm de mercure ;

— suivie, après un temps de latence, d'une variation de pression beaucoup plus ample s'installant progressivement pour atteindre un plateau.

— Dans certains cas, peut survenir une chute spontanée de la variation de pression venant se placer à un nouveau plateau inférieur au premier.

— A la fin de l'émission sonore, il y a d'abord une chute brutale mais faible, suivie d'une chute beaucoup plus lente avec retour à la valeur de repos.

Il semble donc exister deux ordres de phénomènes :

L'un physique :

— immédiat ;

— stable ;

— qui doit être dû à la propagation de la pression de radiation dans les liquides labyrinthiques et qui persiste après la mort de l'animal, ce qui confirme l'élément physique pur.

L'autre biologique :

— apparaissant après un temps de latence, de façon progressive ;

— très ample, mais variable avec le temps ;

— disparaissant progressivement après la mort de l'animal ;

— caractérisé après curarisation par la régularisation du plateau.

A la suite de ces recherches, il nous semble que l'on puisse retenir le fait suivant :

— Il existe deux sources de variations de pression, l'une *initiale* de nature physique (la chaîne tympano-ossiculaire transmettant la pression de radiation), l'autre *secondaire*, biologique, de nature indéterminée, mais déclenchée par la première.

Ces deux sources engendrent une surpression dans les liquides labyrinthiques.

Suivant les conditions d'enregistrement on peut obtenir :

— en l'absence totale de fuite, une pression positive ;

— en présence de fuites ou d'orifice de compensation supplémentaire, la variation *de pression est dérivée vers l'extérieur entraînant un deuxième* mouvement de compensation dans la sonde de mesure et aboutissant à une lecture en variation de pression négative.

— Cette pression est proportionnelle à l'intensité dans certaines limites.

Ceci revient à envisager des circuits hydrauliques complexes à résistance variable conditionnant le sens et l'amplitude des mouvements dans les différentes parties du labyrinthe.

VARIATIONS DE PRESSION AÉRIENNE

En soumettant l'oreille de l'animal à de telles variations de pression aérienne sans signification auditive on constate

A Utricule

Chaine tympano ossiculaire intacte

1° *Pression aérienne statique*

Dans ces conditions les variations sont extrêmement faibles Les valeurs enregistrées ne semblent pas devoir dépasser 4/10 de mm de mercure, et paraissent plus amples en dépression qu'en surpression

2° *Pression aérienne alternative à la pompe*

Les variations sont à la limite de l'appréciation 3 à 6/100 de mm de mercure

Chaine tympano ossiculaire détruite

Dans ce cas après obturation de l'orifice bullaire pour maintenir l'étanchéité on note une très nette augmentation des variations de *pression* Il est nécessaire cependant dans ce cas de faire la part d'une action directe des variations de pression aérienne sur la sonde de mesure à travers une éventuelle fuite

1° *Pression aérienne statique*

Les variations peuvent dépasser 4 mm de mercure et sont plus amples en dépression qu'en surpression

2° *Pression aérienne alternative*

L'amplitude de la déviation bien que faible (7/10 de mm de mercure) est néanmoins beaucoup plus importante que dans les conditions précédentes

Canaux semi circulaires

Les enregistrements effectués au niveau des canaux semi circulaires ont montré des *variations identiques*

Augmentation des variations de pression lorsque la chaine tympano ossiculaire *est détruite* Dans ces conditions l'obturation de l'orifice bullaire accroit considérablement les *variations*

Mouvements dans le même sens *mais* peut être avec un léger décalage dans le temps lors des enregistrements en deux points du même canal selon les techniques de lecture directe déjà décrites

B *Interprétation*

Il semble dans ce cas que l'on se trouve en présence de phénomènes uniquement physiques

Les variations de pression

B. *Interprétation*

L'étude détaillée du tracé permet de constater :

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— suivie, après un temps de latence, d'une variation de pression beaucoup plus ample s'installant progressivement, pour atteindre un plateau ;

— Dans certains cas peut survenir une chute spontanée de la variation de pression venant se placer à un nouveau plateau inférieur au premier ;

— A la fin de l'émission sonore, il y a d'abord une chute brutale mais faible suivie d'une chute beaucoup plus lente avec retour à la valeur de repos.

Il semble donc exister deux ordres de phénomènes :

L'un physique :

— immédiat ;
— stable ;
— qui doit être dû à la propagation de la pression de radiation dans les liquides labyrinthiques et qui persiste après la mort de l'animal, ce qui confirme l'élément physique pur.

L'autre biologique :

— apparaissant après un temps de latence, de façon progressive ;
— très ample, mais variable avec le temps ;
— disparaissant progressivement après la mort de l'animal ;
— caractérisé après curarisation par la régularisation du plateau.

A la suite de ces recherches, il nous semble que l'on puisse retenir le fait suivant :

— Il existe deux sources de variations de pression : l'une *initiale* de nature physique (la chaîne tympano-ossiculaire transmettant la pression de radiation), l'autre *secondaire* biologique de nature indéterminée mais déclenchée par la première.

— Ces deux sources engendrent une surpression dans les liquides labyrinthiques.

Suivant les conditions d'enregistrement on peut obtenir :

— en l'absence totale de fuite, une pression positive ;

— en présence de fuites ou d'orifice de compensation supplémentaire, la *variation de pression est dérivée vers l'extérieur entraînant un deuxième* mouvement de compensation dans la sonde de mesure et aboutissant à une lecture *en variation de pression négative*.

— Cette pression est proportionnelle à l'intensité dans certaines limites.

Ceci revient à envisager des circuits *hydrauliques complexes à résistance* variable conditionnant le sens et l'amplitude des mouvements dans les différentes parties du labyrinthe.

VARIATIONS DE PRESSION AÉRIENNE

En soumettant l'oreille de l'animal à de telles variations de pression aérienne sans signification auditive on constate

A. *Utricule*

Chaîne tympano ossiculaire intacte

1° *Pression aérienne statique*

Dans ces conditions les variations sont extrêmement faibles. Les valeurs enregistrées ne semblent pas devoir dépasser 4/10 de mm de mercure et paraissent plus amples en dépression qu'en surpression.

2° *Pression aérienne alternative à la pompe*

Les variations sont à la limite de l'appréciation : 3 à 6/100 de mm de mercure.

Chaîne tympano ossiculaire détruite

Dans ce cas, après obturation de l'orifice bullaire pour maintenir l'étanchéité, on note une très nette augmentation des variations *de pression. Il* est nécessaire cependant dans ce cas de faire la part d'une action directe des variations de pression aérienne sur la sonde de mesure *à travers une* éventuelle fuite.

1° *Pression aérienne statique*

Les variations peuvent dépasser 4 mm de mercure et sont plus amples en dépression qu'en surpression.

2° *Pression aérienne alternative*

L'amplitude de la déviation *bien que faible (7/10* de mm de mercure) est néanmoins beaucoup plus importante que dans les conditions précédentes.

Canaux semi-circulaires

Les enregistrements effectués au niveau des canaux semi-circulaires ont montré des *conditions identiques* :

- Augmentation des variations de pression lorsque la chaîne tympano ossiculaire est *détruite.* Dans ces conditions l'obturation de l'orifice bullaire accroît *considérablement* les variations.
- *Mouvements* dans le même sens mais peut être ... alage ... anal

B. *Interprétation*

Il semble dans ce cas que l'on se trouve en présence de phénomènes uniquement physiques.

Les variations de pression

— atteignent un rapidement plateau,
— demeurent stables,
— persistent après la mort.

Les résultats confirment le rôle de tampon de la chaine ossiculaire le le rôle de compensation de la fenêtre ronde.

CONCLUSIONS

Il est possible d'engendrer des variations de pression des liquides labyrinthiques notables à l'aide d'agressions vibratoires aériennes On peut supposer que ces variations de pression agissent directement sur les macules utriculaires ou sacculaires, et peut-être aussi sur les crêtes des canaux semi circulaires. Dans certaines conditions, difficiles à déterminer, il semble que ces variations de pression puissent aboutir à des déplacements de liquide

On assiste à une dissociation entre :

— les *variations de pression dues à des sons très intenses*, nécessitant un appareil de transmission normal, et sous le dépendance d'un double mécanisme physique et biologique.
— et les *variations de pression aérienne amples*, mais de très basses fréquences, dont l'action, d'origine uniquement physique semble être maximum sur des oreilles non protégées par la chaîne tympano-ossiculaire, en particulier lorsque la fenêtre ronde n'a plus la liberté d'assurer une compensation suffisante ou encore lorsqu'elle devient elle-même une porte d'entrée

En pratique, il semble que l'on puisse proposer la conclusion suivante .

1) *Si des oreilles normales sont soumises à des sons très intenses* ($>$130 db par cycle sur le tympan, ce qui représente fort heureusement des conditions tout à fait exceptionnelles) elles sont le siège de variations de pression pouvant engendrer éventuellement des troubles de l'orientation et de l'équilibration

2) Les sujets porteurs de lésions de l'appareil de transmission, s'ils sont, en principe, protégés contre les méfaits des agressions sonores très intenses peuvent dans certains cas être vulnérables vis à vis des variations de pression aériennes très amples et de très basse fréquence

SUMMARY

A technic to record the pressure of labyrinthine fluids is described The variations of the labyrinthine pressure were studied with several kinds of stimulations variations of the ambient air pressure and presentation of very loud pure tones Variations of the pressure of labyrinthine fluids during these stimulations were found indeed The origin of these variations is either of a mechanical or of a biologica nature

ZUSAMMENFASSUNG

Eine Methode zur Messung des Labyrinthflüssigkeitsdruckes wird beschrieben Veranderung des auswartigen Luftdruckes und laute Tone geben Anlass zu Veranderung dieses Labyrinthdruckes

Dr M Aubry, 65 Ave Georges Mandel, Paris XVI, France

DISCUSSION

D van Caneghem Je tiens à confirmer les résultats obtenus par MM Pialoux et ses collaborateurs sur l influence des pressions exercées dans le conduit auditif et l influence des sons sur la pression endolabyrinthique — mais chez l homme

Si chez l homme normal on exerce une pression de 10 cm d eau dans le conduit auditif on obtient, en position de Romberg une déviation hétérolatérale de la tete et si on exerce une forte pression de 10 cm de mercure on obtient une déviation homolatérale de la tete — dans le premier cas on excite et dans le second cas on paralyse les terminaisons nerveuses de l utriculus

D autre part chez l homme, il suffit d une légère stimulation acoustique, il suffit que le sujet perçoive le son pour provoquer chez lui une déviation *soit hétéro*-homolatérale de la tête suivant qui la pression que préexiste dans le labyrinthe est normal ou augmentee

Dans les deux cas la deviation de la tete ne se laisse expliquer que par des modifications dans la pression endolabyrinthique modifications qui exercent leur effet sur l utricule dont le stimulant adéquat est constitue par la pression endo labyrinthique

G Portmann Je tiens à feliciter d une façon toute particuliere les résultats obtenus par M Pialoux et je me permets de lui poser deux questions Y a t il une relation physiologique entre ses expériences et le phénomene de Tullio?

D autre part ne pense t il pas que sur le plan, social les modifications de pression tonale ont des consequences pathologiques graves avec la civilisation moderne caractérisée par le developpement désordonné des bruits les plus violents?

P Pialoux (Réponse) Je remercie M van Caneghem de l intéret qu il a bien voulu porter à notre communication

Je remercie M le Prof Portmann de ses très aimables paroles auxquelles je suis très sensible Je pense que l expérience de Tullio procède d un mécanisme voisin mais elle est faite dans des conditions un peu différentes Je suis entièrement d accord sur le problème social posé par le bruit dans la vie moderne Il s agit d un sujet tres vaste qu il me paraît difficile d aborder ici

HISTOLOGICAL, THERMAL AND BIOCHEMICAL EFFECTS OF ULTRASOUND ON THE LABYRINTH AND TEMPORAL BONE

J. Angell James, G. A. Dalton, H. F. Freundlich, M. A. Bullen,
P. N. T. Wells (*Bristol*), D. A. Hughes, J. Chou (*Oxford*)

The action of 3 megacycle ultrasonics on the labyrinth of guinea pigs and sheep is described. Temperature measurements in different parts of the labyrinth during ultrasonic application are reported. Histological and biochemical effects are presented showing characteristic changes in the fluids and in the vestibular and cochlear end organs.

Last year (1962) we described a new 3 megacycle ultrasonic generator for destruction of the vestibular end organ and we referred briefly to some animal investigations which we had undertaken on the sheep.

During the last twelve months we have continued these investigations with the same equipment. The investigations have taken three forms. First, histological effects on the labyrinth of the sheep; second, thermal effects in the human temporal bone; and third, biochemical effects in the endolymph and perilymph of the guinea pig. In all the investigations during the last twelve months the standard 3 megacycle microcone applicator has been used. The methods of application have been the same as those which we employ in treating the labyrinths of patients suffering from Menière's disease. Briefly these consist of the exposure of the lateral semi-circular canal with the bone thinned down to approximately ¼ mm thickness when the grey line shows clearly. Thereafter ultrasound is applied over this area using saline as a coupling and coolant fluid. Irradiation is begun at an intensity of 10 watts/cm² and is increased to a maximum of 22 watts/cm². Application is continued until paralytic deviation of the eyes has been maintained for two minutes and the ultrasound is turned off for fifteen seconds and then reapplied at 22 watts/cm². If the eyes show labyrinthine irritation again the application is continued until paralysis has been maintained for two minutes. A further period of fifteen seconds rest is allowed followed by application again at 22 watts/cm². If no further irritation occurs five further minutes of application at 22 cm² watts is continued and the treatment is completed.

Altogether eighteen investigations have been undertaken in the sheep. In the first seven we used a modified Lehfeldt 1 megacycle apparatus. In the remainder 3 or 5 megacycles were used from the Bristol apparatus. General anaesthesia has always been employed.

In the sheep there is very little pneumatization of the mastoid and it is therefore necessary to expose the facial nerve and follow this to its bend as the landmark for identifying the lateral semi-circular canal. Five of our



Fig 1 Crista of the lateral canal of sheep 8 days after irradiation with 1 megacycle ultrasound

animals died within a few days of the operation and post mortem examination by our veterinary colleagues showed that death was due to stress with adrenal failure Histological studies have so far been made in nine of the survivors Intravital fixation by Wittmaack s method was performed at varying periods after irradiation The temporal bones were sent to Dr C S Hallpike of the Medical Research Council Otological Unit and to him we are deeply indebted for the decalcification preparation and staining of serial celloidin sections and his very helpful comments upon them We have attempted to space out the survival period of the animals into a variable number of weeks as our experience suggests that cells damaged by ultrasound may not show histological changes immediately but may undergo gradual degeneration and death over a period of some weeks after the application

Fig 1 shows a section of the crista of the lateral semicircular canal from an animal in which the post operative vestibular disturbance was more severe than usual and because it was unable to stand we sacrificed it eight days after irradiation at 1 megacycle per second The blood vessels are dilated the neuroepithelium appears to be disorganized and the cuticular membrane is absent The other cristae showed similar changes which correspond very closely to those found by Lumsden and his co workers in the cat

Fig 2 shows the normal sheep s crista for comparison

Fig 3 the utricular macula shows similar changes to those in the crista

It is interesting to note that histological damage to the cochlea in the sheep is frequently heavy in the basal and apical portions We have sometimes observed in the human that after treatment the hearing at the highest and lowest frequencies is made worse while it remains unaltered in the middle of the frequency range We wonder whether the peculiar configuration of the



Fig 2 Section of the normal crista of a sheep

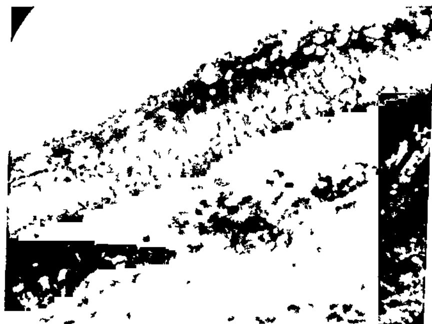


Fig 3 Utricular macula 8 days after irradiation

cochlea happens to concentrate the energy of the internally reflected ultrasound in the apical turns, leaving a less heavily affected middle region The basal turn is the most vulnerable being nearest to the source of energy

Fig 4 shows that at the apex of the cochlea there has been damage and haemorrhage



Fig 4 Cochlea 20 days after irradiation

Temperature Changes in the Human Post mortem Temporal Bone

As a result of our clinical experience we had come to the conclusion that post irradiation facial paralysis was nearly always due to heat conducted through the temporal bone to the Fallopian canal In order to investigate this we performed a series of experiments with isolated human temporal bones with thermocouples inserted in the Fallopian canal the vestibule and the cochlea Saline cooling was used exactly as in the human operation The temperatures recorded at different intensities of ultrasound are shown in Fig 5

In the human being we have found that application of 3 megacycle ultra sound at an intensity of 25–30 watts/cm² with the Bristol apparatus and using the technique described above in 40 operations resulted in two cases of immediate facial paresis and two cases when facial paralysis developed at the fifth or sixth day Since reducing the intensity to a maximum of 22 watts/cm² we have not had a case of facial paralysis from heat in 75 conse cutive operations It would appear therefore from the experiments that the facial nerve can tolerate a temperature of 46°C This is the critical point beyond which damage is likely to occur It is important to remember that the distance of the facial nerve from the lateral semicircular canal is subject to considerable variation as shown by Waltner s investigation of human temporal bones

It was the fact that we have observed in the human being an improvement in hearing after ultrasonic application in 23 % of the cases that led us to speculate on the possibility that the ultrasonic vibrations were increasing the permeability of the endolymphatic system and thus reducing the endo lymphatic hydrops and allowing recovery of function We therefore in



Fig 2 Section of the normal crista of a sheep

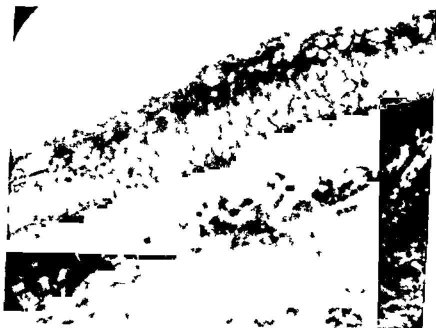


Fig 3 Utricular macula 8 days after irradiation

cochlea happens to concentrate the energy of the internally reflected ultra sound in the apical turns leaving a less heavily affected middle region The basal turn is the most vulnerable being nearest to the source of energy

Fig 4 shows that at the apex of the cochlea there has been damage and haemorrhage

tion of perilymph would be maintained by the flow of C S F through the cochlear aqueduct

In five animals of the present series it was found, to our surprise, that the composition of the endolymph collected from the untreated ear had also changed As far as the small numbers allow judgment, this change appears to be less marked and to be transitory rather than permanent, as in the treated ear It seems possible that it may be related to the sympathetic changes observed in the normal eye in association with disease in the opposite eye

ACKNOWLEDGEMENTS

We are indebted to the Medical Research Council and the United Bristol Hospitals for grants and facilities to Dr Hallpike for the histological studies of the sheep to Professors Messervey and Ottaway and Miss Weaver of the Veterinary Department of the University of Bristol for advice and assistance in the animal work We thank Mr Godman and Mr Hancock of the University of Bristol for the photomicrographs and illustrations

RÉSUMÉ

Nous décrivons l action de 3 Mc/s d ultrasons sur le labyrinthe des cochons d Inde et des moutons

Nous faisons un rapport sur les temperatures mesurées pendant l application d ultrasons aux parties différentes du labyrinthe Les effets histologiques et biochimiques sont présentés montrant les changements caractéristiques dans les fluides et dans les organs vestibulairescochléaires

J Angell James Litfield House, Clifton Down Bristol 8 England

DISCUSSION

C Sjoberg Uppsala At the International Vestibular Symposium 1963 at Uppsala the ultrasound team at the otolaryngological department, University Hospital, presented the results of ultrasonic irradiation on Ménière s disease

In collaboration with Asst Professor J Stahle experiments on pigeons have been done [1] Now I will present these results

We have used our new Swedish Ultrapoint apparatus on pigeons in order to study the functional and histological effects of high frequency ultrasound on the inner ear

The application tips of the transducer have had a diameter of 1 5 and 2 2 *mm* The average dose has been 1 2 watts and the irradiation time has varied between 1 and 20 minutes

The function of the secretory epithelium has been studied through the use of different histochemical staining methods The following results have been obtained

1 Staining with toluidine blue has shown an abundant presence of a metachromatic substance in the labyrinth It takes a red lilac stain, as opposed to non

[1] Dr J Stahle s paper will be published in the transactions of the International Vestibular Symposium which will appear as a suppl of *Acta Oto-Laryngologica* 1964

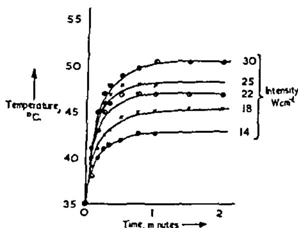


FIG. 5. Graph of heating of Fallopian canal plotted against tissue during irradiation of the lateral semicircular canal with 3 megacycles ultrasound.

vestigated the effect of ultrasound on the ionic composition of the vestibular fluids in a small series of guinea-pigs (thirteen). The vestibular fluids were collected at periods of from twenty minutes up to two days after treatment. Endolymph was collected through the oval window, perilymph through the round window. The collections were made from both treated and untreated ears.

In the endolymph from the treated ear Na^+ concentration increased and K^+ concentration decreased. This was found in all animals except one where, although paralytic nystagmus was apparently produced, the animal recovered and subsequently showed none of the disorders of balance found with the others. It was noteworthy that in only one animal, namely that left for the longest period after treatment, was the utricle collapsed and filled with blood, a condition which we found constantly when we collected fluids from the labyrinth of sheep which had been irradiated some weeks beforehand. In all animals the perilymph in the treated ears remained essentially normal in composition.

These changes are in contrast to those which occur in the perilymph immediately after death, then the Na^+ concentration falls and the K^+ rises, while in the endolymph Na^+ concentration rises and the K^+ concentration falls.

It has recently been shown that the ability of tissues, such as brain, muscle and liver, to concentrate Na^+ and K^+ against electrochemical gradients is rapidly destroyed by ultrasound at intensities comparable to those used for treating the inner ear.

The rapid alterations found in the ionic composition of the endolymph might thus be explained by assuming that the function of some secretory tissue, such as the stria vascularis, has been destroyed. Alternatively, the changes might be due, either solely or partly, to failure of some permeability barrier between endolymph and perilymph. In this case the normal composi-

ON NYSTAGMUS PROVOKED BY CENTRAL STIMULATION

Preliminary note

L. B. W. Jongkees, W. J. Oosterveld and S. Zelig
Amsterdam, The Netherlands

From the E. N. T. Department of the Wilhelmina Gasthuis, University of Amsterdam

The effect of various vestibular influences (alcohol, rotation, calorisation, optokinetic stimulation, necktorsion and parallel swing) on nystagmus, provoked by electric stimulation of the nystagmogenic centre of Bergmann, Lachmann and Monnier is discussed. In some cases pure addition or subtraction of effects results (rotation), in others centrally provoked nystagmus is depressed (alcohol) or increased (optokinetic). Cinnarizine does not influence the nystagmus provoked by central stimulation.

Since 1929 it is known that a nystagmus of the eyes can be obtained by electric stimulation of the mesodiencephalon, but it is especially during the last decade that Bergmann, Lachmann & Monnier (1960) have done a great deal of research work in this field. The nystagmogenic centre appears to be fairly large. In the mesodiencephalon it extends from the frontal part of the reticular formation and from its projection into the intralaminary system of the lateral thalamus towards the mesencephalic reticular formation, medially to the lateral geniculate body. The most sensitive part is concentrated in the thalamic region between the laterodorsal and ventral nucleus, medially from the reticular nucleus and ventrally from the superior colliculus.

Stimulation of this centre at the right gives a nystagmus with the rapid phase towards the left and v. v. The frequency of the beats depends upon the intensity of the stimulus and varies from some beats/min to about 4 beats/sec. A stronger stimulation gives a higher frequency of nystagmus and provokes a longer after nystagmus. After nystagmus is the name for nystagmus beats appearing after the stimulation has been stopped.

The stimulation takes place with the aid of insulated needle electrodes through which 20 to 50 impulses per second with a voltage of 3 to 6 are given.

The reaction of the eyes begins to show itself after a latency time of great variety.

The pattern of the reaction varies greatly between one individual and another but is extremely constant in one and the same animal after a short period of adaptation (about 30 minutes). The nystagmus was recorded by electronystagmography (Hamersma, 1957; Philipszoon, 1959).

metachromatic tissue which stains blue It is found in the cupulae, otoliths and in the cells on the planum semilunatum as well as in the cells on the slopes of the cristae The reaction to staining tells us that this substance contains acidic groups of high molecular weight material

2 The periodic acid Schiff (PAS) reaction shows that these substances are PAS positive, which implies that it is a polysaccharide, mucine This substance takes a clear red stain

The cupulae and otoliths are strongly PAS positive, as is the secretion which covers the cells on the side walls of the cristae Even in the cells of the planum semilunatum and in the transitional epithelium is a PAS positive substance richly present

3 The Alcian blue method finally, gives a clear blue green colour to the cupulae otoliths and numerous cells of the planum semilunatum and in the transitional zone This indicates that acid mucopolysaccharides are present

These investigations have therefore shown that acid mucopolysaccharides are produced from the epithelium of the planum semilunatum as well as from the "transitional" epithelium on the slopes of the cristae

After ultrasonic irradiation the secretory epithelium can more or less degenerate or atrophy and with this the secretion of mucopolysaccharides decreases or disappears

The reduced function in the secretory epithelium, which can always be clearly brought about with ultrasound could possibly be thought to lessen the tendency to labyrinthine hydrops in man In this could lie one explanation for our good clinical results

J Angell James (Reply) In reply to Prof Sjoberg I would like to thank him for the very clear slides and interesting work on the pigeon labyrinth with ultrasound It is not exactly comparable with our own investigation as he has used high intensities and thereby would inevitably induce high temperatures in the bone Some of the histological changes would then be due to the effects of heat We have never observed in our clinical or histological investigation any bone necrosis

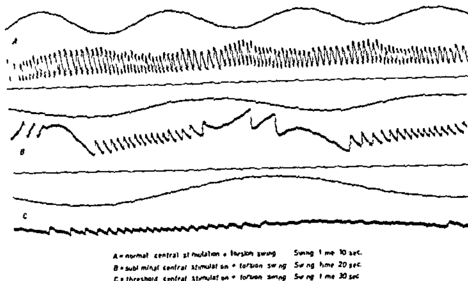
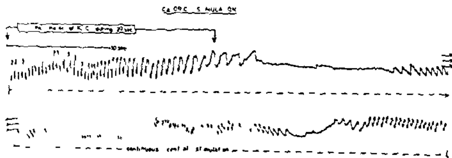


Fig. 3. The interaction of central stimulation and rotatory stimulation on the torsion swing. Permanent central stimulation is combined with the effect of the accelerations on the swing, whose period is indicated by a potentiometer (upper line). *A*, normal strength for both stimuli. B, subliminal central stimulation + angular acceleration at treshold. C, subliminal angular acceleration, central stimulation at treshold.

stimulation. This is shown by a decrease in the total number of beats, the increase of the latency period and a disappearance of the after-nystagmus. The influence of 3.5 cc/kg is still observable after 3 hours and more.

After-nystagmus appears to be the most sensitive part of the nystagmic response to central stimulation. It shows the influence of external influences more clearly and earlier than frequency or latent period.

c. Angular accelerations and central stimulation in their interaction were examined on the torsion swing. Together with recording by electronystagmography this instrument is in use in our department for the routine in



ric stimulation and its effect on centrally provoked nystagmus.

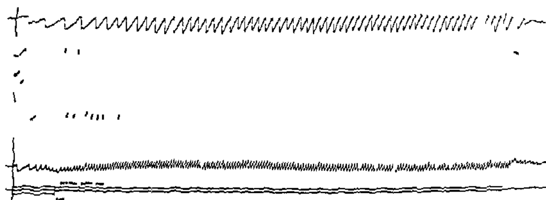


Fig. 1 The nystagmus pattern during central stimulation in five different rabbits. The double line indicates the duration of the stimulation.

In this series of experiments after careful insertion of the needles into the optimal site we stimulated the centre every 5 minutes during 30 seconds. In this way we can go on for hours without any change in the resulting nystagmic response including latency time, frequency and after nystagmus. This allows us to study very closely the effect of various influences on the vestibular labyrinth and system upon central nystagmus.

a Cinnarizine. As Philipszoon has proven cinnarizine is a powerful suppressor of peripheral vestibular function and a good anti seasickness drug. In quantities which strongly affect vestibular function it has not the slightest decreasing effect upon artificial central nystagmus.

b Positional nystagmus following the administration of aethyl alcohol is well known. We studied the influence of positional alcohol and central stimulation on each other. The alcohol was given intravenously, intraperitoneally or orally in various quantities.

We never found any cumulative influence of the nystagmus caused by alcohol in lateral position upon the effect of central stimulation. Aethyl alcohol however has a strong depressive effect upon the responses to central

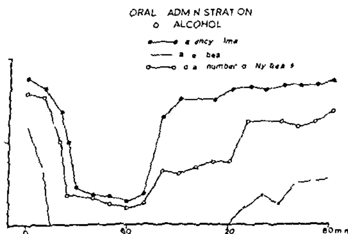


Fig. 2 The effect of oral administration of aethyl alcohol upon the responses to central stimulation. At point O the drug is administered.

PARALLEL SWING

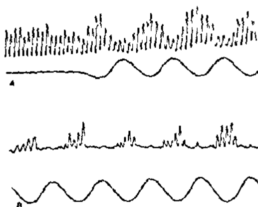


Fig. 6. Combination of linear acceleration and central stimulation. The rabbit is in lateral position on the swing. Continuous central stimulation. The lower line indicates the movements of the swing (potentiometer).

does not clearly influence central stimulation but in case of a subliminal central stimulation necktorsion may bring the effect of central stimulation, (the nystagmus in the corresponding direction) to the surface, not dependent on the nystagmus which the necktorsion itself might have provoked.

g. Linear accelerations. As we proved some time ago, stimulation by linear accelerations can also cause nystagmus. For this purpose rabbits are swung on the parallel swing while lying on their sides. In these cases we generally found some addition and subtraction of linear and central stimulation. With subliminal stimulation for both varieties of stimuli together it was possible in some but not in all cases to provoke a nystagmus if both effects worked in the same direction.

RÉSUMÉ

L'influence de stimulations périphériques diverses (p. e. optocinétique, vestibulaire) sur le nystagmus provoqué par stimulation électrique du centre de Bergmann, Lachmann et Monnier est discutée.

ZUSAMMENFASSUNG

Der Einfluss verschiedener peripharer Reize (z. B. optikinetischer, vestibularer) auf den Nystagmus, erregt mittels elektrischer Reizung des nystagmogenischen Zentrums von Bergmann, Lachmann und Monnier, wird besprochen.

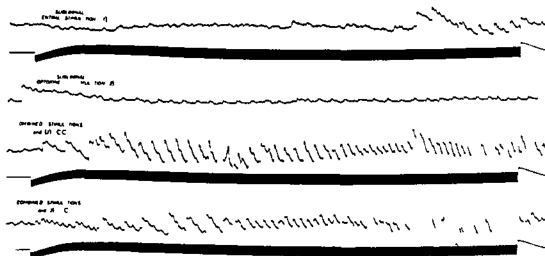


Fig. 5. The combination of subliminal optokinetic stimulation and subliminal central stimulation provokes nystagmus. Its direction does not depend upon the direction (cc = counter clockwise, c = clockwise) of the optokinetic stimulus. The black line indicates central stimulation.

vestigation of rotatory stimulation of the labyrinth. It gives alternatively rotatory acceleration in one and in the opposite direction (de Boer, Carels & Philipszoon, 1963).

The combination of accelerations and central stimulation gives a simple addition or subtraction of the resulting eyemovements. A combination of two subliminal stimuli—i.e. subliminal acceleration and subliminal central stimulation—gives rise to a nystagmus if the two would have led to a nystagmus in the same direction when supraliminal, but should the two stimuli be in opposite directions no nystagmus will appear.

d. Caloric stimulation also influences the effect of central stimulation. Here, however, the effect is not addition or substraction. A caloric stimulus can nullify a central nystagmus for an important period.

If a caloric stimulus is followed (after about 20 sec.) by a central stimulation an increase in frequency of the nystagmus in the direction imposed by the caloric stimulus results. The increase follows in all instances and does not depend upon the nature of the central stimulus (nystagmus to left or right). As soon as the effect of calorisation comes to an end the direction of nystagmus changes again to that imposed by the central stimulus.

e. Optokinetic stimulation was given by placing the rabbit inside a cylinder rotating around it. The black and white stripes on the interior cause a clear and easily recordable nystagmus.

Combination of the optokinetic stimulus with central stimulation gives no addition or substraction but it was found that in case of a subliminal central stimulus the effect of optokinetic stimulation was evident.

A nystagmus in the direction of the central effect became evident and this crossing of the threshold did not depend upon the direction of the optokineetic stimulus.

f. Necktorsion is known to provoke nystagmus (Bos, 1962). This nystagmus

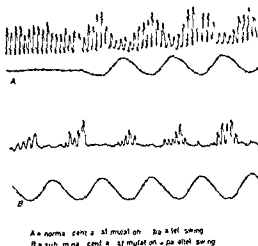


Fig. [illegible]. Combination of linear acceleration and central stimulation. The rabbit is in lateral position on the swing. Continuous central stimulation. The lower line indicates the movements of the swing (potentiometer).

does not clearly influence central stimulation but in case of a subliminal central stimulation necktorsion may bring the effect of central stimulation (the nystagmus in the corresponding direction) to the surface not dependent on the nystagmus which the necktorsion itself might have provoked.

4. *Linear accelerations.* As we proved some time ago, stimulation by linear accelerations can also cause nystagmus. For this purpose rabbits are swung on the parallel swing while lying on their sides. In these cases we generally found some addition and subtraction of linear and central stimulation. With subliminal stimulation for both varieties of stimuli together it was possible in some but not in all cases to provoke a nystagmus if both effects worked in the same direction.

RÉSUMÉ

L'influence de stimulations périphériques diverses (p. e. optocinétique, vestibulaire) sur le nystagmus provoqué par stimulation électrique du centre de Bergmann, Lachmann et Monnier est discutée.

ZUSAMMENFASSUNG

Der Einfluss verschiedener peripherer Reize (z. B. optikinetischer, vestibularer) auf den Nystagmus, erregt mittels elektrischer Reizung des nystagmogenischen Zentrums von Bergmann, Lachmann und Monnier, wird besprochen.

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F. N. Z. Department of the Wilhelmina Gasthuis
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DISCUSSION

F. Brunetti. Je félicite avant tout Mr. Jongkees pour l'importance et l'excellente signification de son remarquable travail. Il est important de rappeler qu'au point de vue clinique les substances neurophysiques (largactil) provoquent les modifications de l'activité de la substance reticulaire et des afférences qui arrivent à ce système provoquent une diminution dans la réponse nystagmique à la stimulation vestibulaire, associée à des altérations qualitatives remarquables (prévalence de la phase lente), des autres produits pharmaceutiques (spécialement les psychotropes) déterminent des modifications mineures. Ces produits peuvents toutefois modifier nettement (pour tout le temps de l'action pharmacologique) les phénomènes d'accoutumence aux stimulations vestibulaires.

Les recherches effectuées dans notre clinique par Buougiova et Hahn ont mis en évidence des phénomènes analogues par effet des stimulations sonores.

F. C. Ormerod. Ormerod congratulated Prof. Jongkees on his paper this morning and on the experimental work which he had described, and which was of the same high standard as we have always had from Utrecht and from Amsterdam. Yesterday he, the speaker, had attempted to describe the effects of visual, mental and psychic processes on nystagmus, this morning Prof. Brunetti had described the effects of injecting acetylcholine and anticholinergic substances into the rabbit on artificially produced nystagmus. Prof. Jongkees had carried out the next step, which correlated the effects of stimulating the central nucleus controlling nystagmus and stimulating the labyrinth by the usual methods at the same time. The results of these three series of experiments when considered together should help to clarify the understanding of the central processes concerned in nystagmus.

He asked Prof. Jongkees if there was a likelihood that in his experiment there was a stimulation of the oculomotor centres as well as or instead of the nystagmus centre.

G. F. Greiner. Je voulais féliciter mon ami Jongkees pour son très intéressant travail et attirer surtout l'attention sur les déductions cliniques qu'il permet. En

effect lorsque nous examinons un malade présentant un nystagmus spontané nous faisons exactement la même dose que Jongkees en stimulant son appareil vestibulaire soit par l'épreuve calvénique, soit par la stimulation rotatoire pendulaire et nous constatons que cliniquement les choses se passent comme dans l'examen de laboratoire Il y a addition ou sous traction ou superposition du nystagmus provoqué et spontané Ce qui est particulièrement intéressant c'est de constater que par contre la torsion de la colonne cervicale ne modifie pas le nystagmus central — c'est là un point qui d'être retenu et vérifié Je pense que la comparaison des résultats expérimentaux avec les réponses cliniques peut apporter une quantité de renseignements et qu'elle ouvre des perspectives qui me paraissent prévues d'avenir

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University of Amsterdam The Netherlands

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Fig. 1

riches en sarcoplasma que ces dernières dans le segment médian intra capsulaire elles sont plus larges leur striation persiste moins nette et elles apparaissent constituées par un cylindre de protoplasma granuleux, renfermant des myofibrilles peu nombreuses et parsemé de noyaux sphériques ou ovoïdes et de chondriosomes en bâtonnets courts La capsule fibreuse est une gaine tubuleuse formée de plusieurs lamelles collagènes concentriques entre lesquelles se logent des cellules conjonctives endothéliformes Extérieurement la capsule se raccorde au tissu fibreux interfasciculaire intérieurement elle répond aux faisceaux de Weissmann dont elle est séparée par un espace rempli de liquide et cloisonné par des tractus conjonctifs qui rejoignent les formations conjonctives environnant le ou les faisceaux de Weissmann On trouve fréquemment une artériole qui fournit entre les fibres et dans leurs gaines pellucides un réseau capillaire à mailles rectangulaires comme dans le muscle même

Sur des coupes transversales et longitudinales Landau a retrouvé les fuseaux — notamment dans le muscle thyroarytenoidien externe (*plica vocalis*) — et tels qu'ils ont été décrits dans l'ouvrage d'histologie de O Bucher (*Histologie* Huber Berne 1948)

Roberto avait déjà bien voulu nous confier ses recherches et ses coupes histologiques

LES FUSEAUX ET LES GLOBES SENSITIFS DU LARYNX

J. Terracol et P. Ardouin
Montpellier et Tours, France

Les auteurs interprétant certaines images de coupes histologiques intéressant le muscle de la corde vocale, étudient la disposition morphologique de quelques terminaisons nerveuses décrites sous le nom de fuseaux neuro-musculaires ou de globes *sensitifs du larynx*.

En dehors de leur appareil nerveux classique, les muscles striés renferment des dispositifs dont la structure indique la spécialisation pour des fonctions sensibles très particulières: ce sont les *fuseaux neuro-musculaires* (Kuhne 1863). Ces organes manquent chez les Poissons et chez les Amphibiens urodèles; *ils existent chez les Amphibiens* anoures, les Reptiles, les Oiseaux, chez les Mammifères et chez l'Homme. C'est dans cette dernière classe qu'ils ont été le mieux étudiés.

Dans un travail paru dans les *Acta anatomica* (vol. 30, n° 1–4, 19[illegible]) E. Landau avait primitivement enseigné, en s'appuyant sur les travaux de J. Schaeffer (1920), que les fuseaux neuro-musculaires, organes fusiformes longs de 2 à 3 mm, qui gardent dans leur intérieur un certain nombre de fibres musculaires *minces qui présentent parfois* un caractère embryonnaire et dans lesquels se terminent de nombreux nerfs et vaisseaux, n'existent pas dans le larynx, ni dans le muscle diaphragme, ni chez les vieillards. Autrement dit, ils pourraient disparaître avec la sénescence[1].

Mais ultérieurement G. Winckler ayant découvert des fuseaux neuro-musculaires dans le muscle diaphragme, E. Landau reprit l'étude du larynx humain.

On doit se poser une question:

Qu'est-ce exactement qu'un fuseau neuro-musculaire?

Les histologistes avec Georges Dubreuil considèrent qu'un fuseau neuro-musculaire est formé par plusieurs fibres musculaires spéciales grêles parallèles, dites fibres fusales, groupées en un ou plusieurs faisceaux de deux à cinq fibres. A chacune d'elles sont associées deux terminaisons nerveuses, l'une *motrice*, l'autre *sensible*. Une capsule fibreuse enveloppe la région moyenne et envoie dans le fuseau des cloisons et des gaines pellucides qui entourent les fibres. Les fibres fusales sont groupées en faisceaux de Weissmann; elles sont grêles et ont une direction parallèle à celle des fibres musculaires proprement dites beaucoup plus volumineuses; dans leur portion extracapsulaire, c'est-à-dire à leurs extrémités, elles présentent la double striation longitudinale et transversale des fibres striées, mais elles sont plus

[1] On lira avec profit la bibliographie qui termine le travail de E. Landau.



Fig. 3

Quant aux fibres myélinisées et colorées par le procédé de Weigert (modifié par L. Landau) l'histologiste de l'Institut Galli Valerio note que sur une même coupe la gaine de myéline est variable et ceci très souvent. Une même fibre isolée peut être entourée par une gaine de myéline différente selon les points en aspect et en épaisseur. Dans la gaine de myéline les entonnoirs décrits par Schmidt Lautermann peuvent sur une même fibre présenter une épaisseur variable et même changer d'épaisseur. Tantôt les bords sont latéraux et éloignés du cylindraxe, tantôt les entonnoirs s'unissent intimement par leurs bords et sur une même ligne, tantôt sur une seule partie de la fibre à un point tel que le cylindraxe est entouré par la gaine de myéline en une couche homogène. Il est évident, écrit l'auteur, que cette variabilité dans l'aspect a une cause et que toutes les suppositions, sans les conclusions formelles de l'expérimentation, sont permises.

Cette phrase vérifie une fois de plus notre pensée constante. En l'état actuel on ne sait rien ou presque rien sur la neuro-physiologie du larynx malgré les travaux remarquables de Sir V. H. Negus, de Ruedi et d'autres auteurs. C'est un organe terriblement compliqué. Sa formation, si l'on peut dire, est tumultueuse. Ceci par le seul fait que c'est un organe dérivé de plusieurs arcs branchiaux et du système cardiaque. Les recherches montrent que par certains côtés la physiologie du larynx permet d'envisager une ressemblance fonctionnelle étroite entre la neurophysiologie du coeur et celle de la corde vocale : la systole et la diastole, la contraction et la dilatation du sphincter glottique.



Fig. 2

Les recherches de W. Racine sur l'innervation végétative et sensitive du *larynx, principalement des cordes vocales*[1] ont *confirmé* sur ce point le travail de V. Roberto.

Cet auteur avait souligné le rôle des *corpuscules tactiles* (Verson) ou *tasts goblets* (Schofield) ainsi dénommés parce que ce sont d'après lui des bourgeons accessoires de la gustation et qu'on les retrouve dans les papilles caliciformes linguales, à la pointe de la langue (Wellauer) et sous la langue.

V. Roberto a retrouvé un tel corpuscule dans le repli aryténo-épiglottique et dans l'épiglotte : un « *gomitolo sensitivo* », *soit un peloton de fibres nerveuses* et devenu, quand il est plus volumineux, un *globo sensitivo*. Autrement dit, ce sont des *corpuscules sensitifs*.

En poussant plus avant ses recherches, I. Landau a découvert dans la sous-muqueuse d'un larynx humain, à l'entrée du ventricule de Morgagni, une formation riche en nerfs et ceci sur douze coupes.

Ce fait a retenu l'attention du chercheur. I. Landau a demandé l'avis de plusieurs de ses *collègues spécialisés, notamment le professeur J. P. Tallens*. Le résultat de la consultation, si l'on peut dire, fut le suivant : le tissu est normal, seule l'origine exacte demeure douteuse.

Landau et Coll. ont retrouvé une formation à peu près semblable dans la sous-muqueuse de la corde vocale. Peut-être s'agissait-il d'un fuseau neuro-musculaire ?

[1] Racine W. — Le système nerveux végétatif du larynx. *Practica oto-rhino-laryng.* (Basel) 7, 1945.



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FIG 2

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Landau et Coll ont retrouvé une formation à peu près semblable dans la sous muqueuse de la corde vocale Peut être s'agissait il d'un fuseau neuro musculaire?

[1] Racine W — Le système nerveux végétatif du larynx *Practica oto rhino laryng* (Basel) 7, 1945

TEMPERATURE MEASUREMENTS IN THE RESPIRATORY TRACT OF LARYNGECTOMIZED PATIENTS[1, 2]

G. A. SCHULTHESS
Zurich, Switzerland

From the Department of Otolaryngology (Head: Prof. L. Ruedi), University of Zurich

Two phenomena are described which can be observed in laryngectomized patients with simultaneous and continuous recording of nasal temperature and respiratory rate.

1. There is an air flow through the nose of the laryngectomized patient synchronous with respiration and heart beat which may account for the function of smell of these individuals.

2. On insufflation of the nose with different amounts of air at different temperatures the respiration reacts with a lower rate, other types of reaction being inconstant. This reflex is in close relation to others described by Kratschmer and Sercer.

The laryngectomized patient, because of his altered anatomy of respiration, affords an excellent opportunity for the study of the physiologic problems of respiration and heat moisture exchange.

The variation in the results of the temperature measurements in the respiratory tract of both normal and laryngectomized patients previously reported by Koch's group at Lund (1958), Cole (1954), Heyden (1950), Schwab (1955), Scuderi (1951), Sercer (1936, 1952) and others is very understandable when the many varying factors involved are recognized. The reaction of the respiratory tract to heat, to moisture and to environmental influences is subject to continuous change. Furthermore, the measurement of temperature and the actual recording of results is itself a delicate problem.

The purpose of this paper is to demonstrate two simple phenomena related to the temperature of the airway. These are based on continuous and simultaneous measurements with single test persons.

Obs. No. 1

The temperature is picked up with a thermistor from the nose at the level of the piriforme apert[illegible] illustrates the doul le [illegible] actual temperature an[illegible] around it. The rhythm of respira

[1] These studies were partly supported by Fritz Hoffmann La Roche Stiftung, Zurich, Switzerland.

[2] With the collaboration of the Institute of Chemical Engineering and Cryogenics (Head: Prof. I. Grassmann), Swiss Federal Institute of Technology.

SUMMARY

The authors in interpreting some pictures of histologic sections of the vocal cords, describe the morphologic appearance of some nerve endings described as neuro muscular spindles or sensitive globules of the larynx

ZUSAMMENFASSUNG

Die Verfasser erläutern gewisse Bilder der histologischen Schnitte der Stimmbändermuskeln Die Struktur der Nervenendungen, als neuro muskulärischen Spindeln und sensitiven Kugeln beschrieben, wird besprochen

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42, Bd Bé

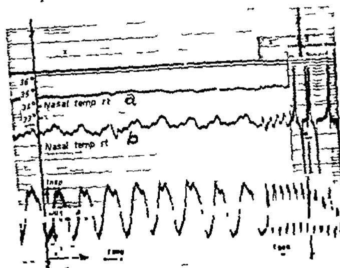


FIG 2 Temperature fluctuations in the nose of the laryngectomized patient

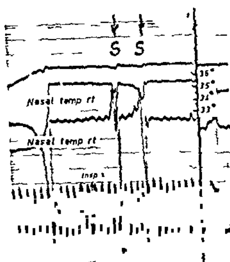


FIG 3 Nasal temperature response with swallowing

irritation of the nasal mucosa by chemical or physical agents provokes an expiratory stop of respiration in different test animals Occasionally we found the same respiratory stop on application of an air flow of 12 l/min through the nose of a laryngectomized patient (Fig 4) This reaction corresponding to the Kratschmer reflex may be just a fright reaction in our limited number of observations Kratschmer insists that his reflex is transmitted on the afferent conduction through the trigeminal nerve He also observed this reaction after cutting the vagus nerve

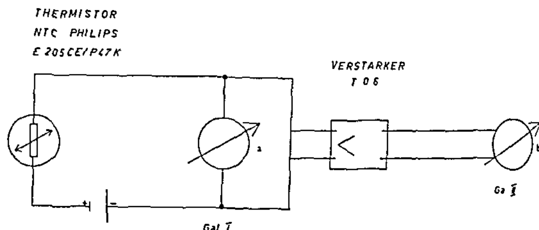


Fig 1 Diagram of circuitry for temperature measurements

tion is recorded as follows A shield is placed on the region of the xiphoid process of the recumbent patient which synchronously with the respiration interferes with the beam influencing a photosensitive cell thus recording the movements of respiration (Fig 2)

We find that the nasal space of laryngectomized patients is under continuous temperature fluctuation synchronous with the respiration and the heart beat (Fig 2) The change in temperature is about 0 15°C and may range up to 1°C with the action of swallowing This corresponds to about 1/20 to 1/50 of the normal amount of nasally ventilated air This phenomenon does not appear in a nose obstructed at the level of the nares and must therefore be the expression of volume variations in the pharynx and the upper esophagus which cannot expand through the obstructed nasal opening Thus a correlation to other temperature phenomena (e g radiation) can be excluded The temperature response to swallowing (Fig 3 S) demonstrates two definite phases The first phase is a lowering of temperature corresponding to an inward movement of surrounding air at room temperature The second phase is an outward movement with a rise in temperature at the level of the nasal opening We cannot say how this constantly observed reaction and occasionally more complicated patterns really are related to the act of deglutition You may notice that in the laryngectomized patient the act of swallowing is mostly independant from the respiration a fact which has been mentioned by Martin (1963) as a reason of difficulties with decannulation in children The demonstrated air movement in the nose of the laryngectomized patients may at least partially account for their normal sense of smell especially with eating as observed by *Kindler & Ulrich (1959)* and earlier by Bayer

Obs No 2

A reflex correlation between the nasal mucosa and the bronchi called naso pulmonary reflex has been mentioned by Sercer in 1952 It is in close relation to a reflex described by Kratschmer in 1870 who found that the

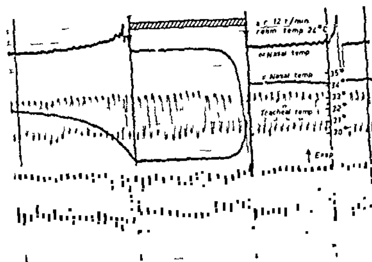


FIG. 5. Lower respiratory frequency on application of an air flow through the nose.

air administered in gradations from 23° to 11°C or warm air at 40°C resulted in a more or less marked retardation of the respiratory rate. The occasionally observed tendency to a diminished respiratory amplitude could possibly correspond to Sercer's observation of a broncho-dilatative reaction with strong physical stimulation. A phenomenon correlating with the broncho-constrictive effect of small irritations was not observed. With smaller amounts of air flow the frequency response became less important and at 4 l/min was completely absent. A reason for the discrepancy of our results and those of Sercer might lie in the measuring devices or in the fact that this author utilized intermittant air pulses.

The activation of Kratschmer's reflex, the naso-pulmonary reflex of Sercer and the reduction of respiratory frequency through artificial insufflation of the nose in the laryngectomized patient must have in common the afferent part of the reflex arch in the trigeminal nerve. In his explanation of the reflex Sercer favored a complex mediation by the thoracic, diaphragmatic and bronchial muscles thus including the vagus nerve. Kratschmer denies the cooperation of the vagus nerve for his reflex. We think that the slowing of the respiratory rate as observed in our cases is not dependent upon the vagus nerve either.

With these experiments we like to stress the necessity of continuous experiments in order to study the naso-bronchial function in laryngectomized patients and to draw further conclusions relating to respiratory function. Special attention should be paid to the methods of recording and to the avoidance of foreign influences which could disturb the results.

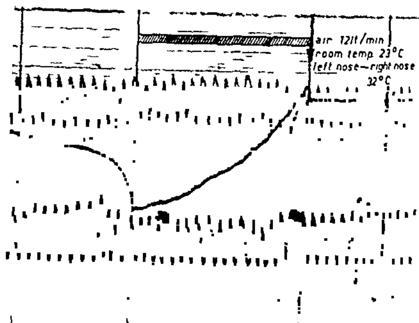


Fig 1 Expiratory stop of respiration on application of an air flow through the nose of a laryngectomized patient

Sercer, on the other hand, observed definite contractions of the homolateral bronchi on irritation of the nasal mucosa of one side These he felt were mediated through the trigeminal nerve A weak irritation provoked a contraction of the bronchial muscles resulting in a narrowing of the bronchial lumen and conversely a strong irritation caused a dilatation The respiratory pattern showed an elevation of the expiratory maximum thus indicating an increased pulmonary pressure and a more efficient ventilation of the lung The rate of respiration was not influenced in Sercer s experiments

On repeated experiments with continuous insufflation of different volumes of air at 23°–25°C we observed a tendency for the temperature of the inspired and expired air at the tracheostoma to rise (Figs 4 and 5) This elevation seems to be the consequence of a lower respiration frequency (Fig 5) The respiratory amplitude was diminished in many instances as in the present case (Fig 5) In others, the elevation of the expiratory level as described by Sercer could be observed However, none of these symptoms were as constant as the diminution of the respiratory rate This reaction persists in most instances as long as the irritation is applied In some cases, lasting somewhat longer but in all cases there is complete return to the previous frequency

In order to ascertain whether the irritant was the insufflated air itself or the temperature or both, a patient operated two months before was tested alternatively with cold and warm air at the constant volume of 12 l/min A recovery time of 5 min was utilized between each test Before entering the nose, the air passed through a coil lying in either acetone with dry ice for cooling or hot water for warming There is no doubt of the invariable reproduceability of the reflex of the lower rate of respiration Either one, cooled

DISCUSSION

F C Ormerod He asked the speaker if it was his experience that in such patients the nasal mucosa and that of the paranasal sinuses was particularly healthy, more so than before the laryngectomy — an example perhaps of improvement from disuse

G von Schulthess (Reply) to Ormerod I can confirm the experience of Dr Ormerod laryngectomized patients show a change in the aspect of the nasal mucosa and seem to be less susceptive to colds

ZUSAMMENFASSUNG

Es werden zwei Phänomene beschrieben, die durch simultane und kontinuierliche Temperatur- und Atmungsregistrierung beim Laryngektomierten beobachtet werden konnen

1 Beim Laryngektomierten besteht eine atem- und pulssynchrone Ventilation des Nasenraumes, die evtl fur die Riechfunktion von Bedeutung ist

2 Die Insufflation unterschiedlicher Luftmengen von verschiedenen Temperaturen in die Nase wird mit einer Herabsetzung der Atemfrequenz beantwortet Dieser Reflex ist verwandt mit ähnlichen, die Kratschmer und Sercer fruher beschrieben haben

RÉSUMÉ

L'enregistrement simultané chez des laryngectomiés des températures nasale et trachéale d'une part, de la fréquence respiratoire d'autre part permet d'observer les deux phénomènes suivants

1 L'air contenu dans les cavités nasales du laryngectomié se meut d'une façon continue, synchrone tant aux mouvements respiratoires qu'aux battements cardiaques

2 L'insufflation dans le nez de quantités d'air variables à des températures diverses entraine une diminution de la fréquence respiratoire Il s'agit là d'un réflexe en relation avec ceux décrits par Kratschmer et Sercer

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Dept of Otolaryngology
University of Zürich Zürich Switzerland

anatomical specimen embedded in a block of wax and the appearances compared Tomographic cuts of both specimens were made in various projections both standard and specifically to demonstrate the fenestra ovalis Serial *tomographic cuts of 1 mm thickness taken 2 5 mm apart* were used for more accurate interpretation of the interrelationship of the superimposed details seen on the plain films

Radiographic Anatomy

In the true anteroposterior position the window is viewed almost tangentially and it can be seen immediately that it is only the 1 mm depth of the window which is seen in this projection The window lies beneath the horizontal semicircular canal and is seen end on in Fig 1 A slight degree of rotation has presented a more open face and the tangential appearance is lost At the same time the facial canal lying immediately lateral to the metal marker creates an oval shadow which might be confused with the oval window The appearances seen in Fig 1 correspond closely to those seen in the transorbital projection of Portmann & Guillen (1959)

Lateral Position

The *end on* view of the lead filled oval window in the lateral projection is mainly of interest to show the downward facing appearance of the oval window and it is obvious that in most instances a plain film *in* the lateral projection can contribute little to the study of the oval window because *of the density of the* superimposed petrous bone Nor are conventional lateral projections (Law 1920 Schuller 1905 Rundstrom 1935 Meyer 1930) with the different tube angulations likely to assist in this study

Submentovertical Projection

Provided the exposure is *correct it* is possible to locate the site of the oval window in this projection but Fig 2 indicates how critical this aspect of the investigation is *and that because* of bony superimposition no real assessment of the margins of the window *or of* its dimensions can be obtained from this position

Stenvers Position

Stenvers position (1917) is a *commonly* used projection for the petrous bone and the site of the oval window is shown in Fig 3 It will be appreciated that although the window is viewed almost *en face* in this projection it lies immediately over the vestibule and can only be appreciated as a darker shadow superimposed on the shadow of the vestibule Also because of the downward tilt of the window the Stenvers projects it obliquely and its true vertical diameter is not appreciated

THE RADIOLOGY OF THE OVAL WINDOW

ERIC SAMUEL, A. F. MACDONALD and A. MARAN
Edinburgh, Great Britain

From the Departments of Diagnostic Radiology and Otorhinolaryngology, Royal Infirmary, Edinburgh

The increasing importance of the radiological demonstration of the petrous bone is emphasized, and the radiographic anatomy, with especial reference to the fenestra ovalis, is described. The various radiographic techniques to demonstrate the oval window are demonstrated, using a specimen bone with lead outlining the fenestra. A further study of a new radiographic position for tomography of the oval window is described, and an indication of its clinical application made.

The evolution of the operating microscope and the development of the surgical treatment for deafness have refocused attention on the stapes and the oval window. It is perhaps not fully appreciated the extent to which radiology can help in the demonstration of the oval window, and the diagnosis of lesions in or adjacent to it. The purpose of this communication is to demonstrate the radiological anatomy of the oval window on anatomical specimens and to relate these appearances to those in normal and pathological human subjects. The techniques and methods which have been found to be most suitable for the demonstration of the oval window will be discussed.

Anatomy

The oval window lies on the medial aspect of the middle ear, on the vestibule, with its maximum diameter in a horizontal plane, its narrower diameter in a vertical plane, and facing out and slightly downwards. The round window lies at an angle of 30° to the oval window and lies on the basal turn of the cochlea.

The oval window lies a few millimetres anterior to the ampulla of the lateral semicircular canal. Whilst in anatomical specimens or dissections the identification of the oval window is relatively easy, in radiographs special projections are needed because the vestibule, the lateral semicircular canal, the facial and the basal turn of the cochlea all closely approximate in this area of complex anatomy and may give rise to confusing appearances.

To allow orientation of the window, a fresh specimen of the temporal bone was dissected, the oval window filled with wax and a small piece of lead foil was fixed into the wax, filling the oval window. Radiographs of this marked specimen were then taken in the conventional radiographic projections and the appearances of the oval window in each projection assessed. These appearances were used to orientate radiographs of another unmarked

anatomical specimen embedded in a block of wax and the appearances compared. Tomographic cuts of both specimens were made in various projections, both standard and specifically to demonstrate the fenestra ovalis. Serial tomographic cuts of 1 mm thickness, taken 2.5 mm apart, were used for more accurate interpretation of the interrelationship of the superimposed details seen on the plain films.

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In the true anteroposterior position the window is viewed almost tangentially and it can be seen immediately that it is only the 1 mm depth of the window which is seen in this projection. The window lies beneath the horizontal semicircular canal and is seen end on in Fig. 1. A slight degree of rotation has presented a more open face and the tangential appearance is lost. At the same time the facial canal lying immediately lateral to the metal lie marker creates an oval shadow which might be confused with the oval window. The appearances seen in Fig. 1 correspond closely to those seen in the transorbital projection of Portmann & Guillen (1959).

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The end on view of the lead filled oval window in the lateral projection is mainly of interest to show the downward facing appearance of the oval window and it is obvious that in most instances a plain film in the lateral projection can contribute little to the study of the oval window, because of the density of the superimposed petrous bone. Nor are conventional lateral projections (Law, 1920; Schuller, 1905; Rundstrom, 1935; Meyer, 1930) with the different tube angulations likely to assist in this study.

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Provided the exposure is correct, it is possible to locate the site of the oval window in this projection, but Fig. 2 indicates how critical this aspect of the investigation is and that because of bony superimposition, no real assessment of the margins of the window or of its dimensions can be obtained from this position.

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FIG 1 Antero posterior view of the oval window demonstrating the end on view of the oval window



FIG 2 Submento vertical view of anatomical specimen with oval window outlined with lead foil

Rossi Position

Rossi & Bisceglie (1962) have suggested another projection specifically to show the oval window (Figs 4, 5 and 6). This is performed in the postero anterior position, the head being placed with the sagittal plane inclined 45° to the vertical and the base line tilted 30°–35° upward. The incident beam is centred 5 cm above and medial to the contralateral external meatus and the emergent ray passing through the ipsilateral external meatus. In this position the oval window is thrown partly over the petrous bone and partly



Fig 3 Stenvers position demonstrating the oval window



Fig 4 Dried skull in Rossi's position demonstrating the incident beam



Fig 5



Fig 6

Figs and 6 The position of the skull from the vertex and side view in Rossi s position

over the translucency of the vestibule and its outline can be clearly seen (Fig 7)

The bony wall surrounding the oval window is however partly obscured by the superimposition of the density of the petrous bone The landmarks most easily recognized are the tegmen the styloid process and the ill defined translucency of the cochlea



Fig 7 View of anatomical specimen in Rossi's position demonstrating the full face view of the oval window

The diverging limb of the basal turn of the cochlea and the ampulla of the lateral semicircular canal form an inverted Y and the vertical limb of the Y leads to the oval window

Tomography

Undoubtedly in all projections the overlap shadows of the petrous bone make the recognition of the outline of the oval window difficult Various authors (Agazzi Cova & Senaldi 1958) Mundnich & Frey 1959 and Rossi & Bisceglie 1962) have advocated tomography as a means of obliterating these unwanted shadows and demonstrating the outlines of the oval window more clearly

The comparison of the tomograms of the lead labelled specimen and an unlabelled petrous bone make it possible to evaluate the anatomical features of the oval window

(a) *Postero-anterior Position*

The postero anterior tomographic cuts which are technically the easiest to perform emphasize the length of the long axis of the fenestra because it appears in three cuts 1 mm apart but actual appreciation of the long diameter is impossible because in any one cut only the short axis can be accurately estimated The relatively paper like thinness of the bone separating it from the facial canal can also be appreciated



Fig. 8. Tomographic study in Rossi's position demonstrating the full face view of the oval window.

(b) *Stenvers Position*

Mundnich & Frey (1959) utilize this position to visualize the foramen ovale but again, as with conventional methods, some foreshortening of the oval window occurs and the oval window appears as a slit rather than as a true oval structure.

(c) *Rossi Position*

Tomographs in this position demonstrate the oval window quite clearly but interpretation of the appearances can be quite difficult. Figure demonstrates the tomographic cut through the oval window, and the outline of the oval window is fully seen. Care is needed not to confuse the shadow with that of the vestibule (Figs. 8 and 9). It will be seen (Fig. 8) that this position clearly demonstrates the jugular foramen.

The level of cut necessary is 1 mm anterior to the level of the vestibule and can be recognised because in this position the plane of the tegmen tympani is immediately posterior, and the plane of the basal turn of the cochlea is immediately anterior to that necessary. Also at this level the course of the carotid canal is seen most clearly at the petrous apex. It is therefore apparent that any sclerosis immediately adjacent to or surrounding the oval window should be recognizable as an abnormal density or encroachment on the actual dimensions of the foramen.

Further study on normal and abnormal petrous bones in the living subject is therefore being carried out, first to become familiar with the normal variation of appearances, and second to assess how early actual pathological change can be detected.

ZUSAMMENFASSUNG

Die immer anwachsende Wichtigkeit der radiologischen Darstellung des Felsenbeins wird betont und die radiographische Anatomie mit besonderer Bezugnahme



Fig 9 Tomographic film demonstrating the oval window and the vestibule The X formed by the lateral semicircular canal and the basal turn of the cochlea are clearly seen

auf das Vorhofsfenster wird beschrieben Die verschiedenen radiographischen Techniken zur Darstellung des Vorhofsfensters werden demonstriert, unter Benützung eines Knochenmodells in dem das Fenster mit Blei umrahmt ist Eine weitere Studie einer neuen radiographischen Position für Tomographie des Vorhofsfensters wird beschrieben und ein Hinweis wird gemacht auf seine klinische Anwendung

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Dept of Diagnostic Radiology and Otorhinolaryngology
Royal Infirmary Edinburgh Scotland

DISCUSSION

G Herberts I was very interested in your demonstration Dr Samuel, as we have studied the X ray picture of the temporal bone by the same technique as you have

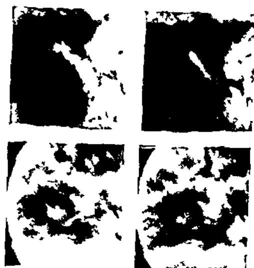


Fig. 1. Tomogram of the cochlea. *Below*: Normal picture. *Above*: From a case of osteogenesis imperfecta.

used—tomography with the Polytom. The technique was worked out by Dr I. Stener working in the radiological department in Gothenburg. We also found that we could get a good picture of the cochlea by tomography in special projections. We started a few years ago using steel wire in cases of stapedectomies as an arrow marking the site of the oval window.

I will show a picture demonstrating the typical changes in a series of seven consecutive cases of osteogenesis imperfecta. On the picture you can see both the normal configuration of the cochlea and the changes of the cochlea with defects of the wall in a case of osteogenesis imperfecta (fig. 1). We think these x-ray changes well correspond to the histopathological findings in osteogenesis imperfecta described by Nager, Altman and others.

At operation we found a normal middle ear and a normal ossicular chain with a mobile stapes, but movements of the stapes did not give any reflex in the round win-

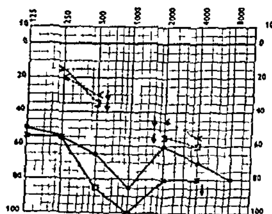


Fig. 2. Audiogram showing loss of bone conduction for the speech frequencies.

dow The audiogram in this case showed a marked loss of bone conduction but as you see the discrimination was relatively good (73 %), (Fig 2)

The audiological test results, the radiological changes demonstrated in the tomogram and the findings at the operation in this case can in our opinion be explained by a hindrance of the sound transmission in the cochlea

We think that the method can also be of value for studying the changes in cases of otosclerosis with severe combined hearing loss

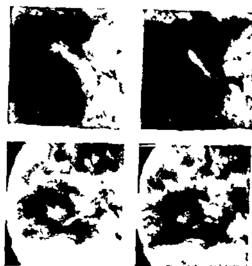


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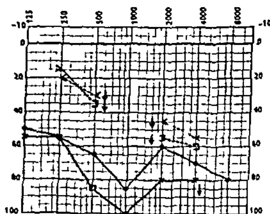


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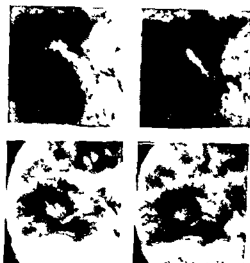


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I will show a picture demonstrating the typical changes in a series of seven consecutive cases of osteogenesis imperfecta On the picture you can see both the normal configuration of the cochlea and the changes of the cochlea with defects of the wall in a case of osteogenesis imperfecta (fig 1) We think these x ray changes well correspond to the histopathological findings in osteogenesis imperfecta described by Nager, Altman and others

At operation we found a normal middle ear and a normal ossicular chain with a mobile stapes, but movements of the stapes did not give any reflex in the round win

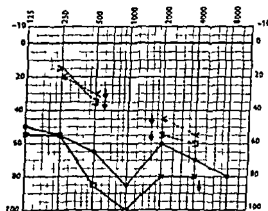


Fig 2 Audiogram showing loss of bone conduction for the speech frequencies

ow The audiogram in this case showed a marked loss of bone conduction but as u see the discrimination was relatively good (73 %), (Fig 2)

The audiological test results, the radiological changes demonstrated in the tomo am and the findings at the operation in this case can in our opinion be explained y a hindrance of the sound transmission in the cochlea

We think that the method can also be of value for studying the changes in cases otosclerosis with severe combined hearing loss

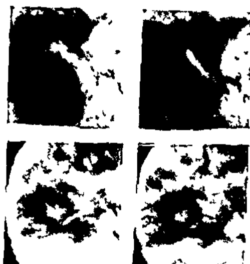


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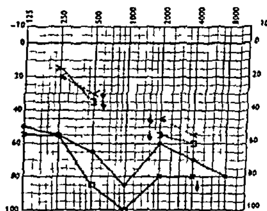


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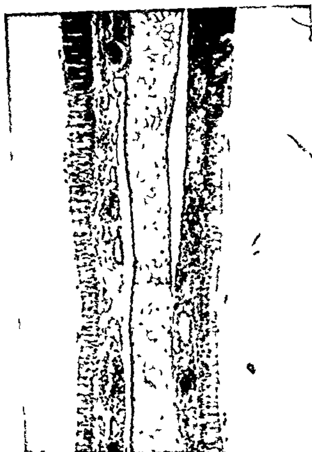


Fig 1

to vascular reactions in the form of vasoconstriction and later on of vasodilatation Both these reactions represent a distinct shifting of the physiological tonus of the blood vessels which must necessarily have a repercussion on the other parts of the mucous membrane and on the metabolism of the tissue Vasodilatation and consecutive hyperemia cause the transudation of the liquid the standstill of which leads to the disarrangement of the metabolism between the cell and its surroundings We suppose that such a changed metabolism conditions the decreased function of the highly differentiated elements of the glands and the epithelium of the mucous membrane of the nose In this way in case the cold is continual it may come to the breach of all physiological mechanisms of the mucous membrane of the nose and the cold air can affect the lower respiratory tracts directly and produce a series of pathological reactions

After the lowering of temperature in the nose in case favourable external conditions set in normalization of the temperature in the nose takes place within an hour The nasal mucous membrane has an extremely strong power of regeneration and reparation

DAMAGE OF THE RESPIRATORY MUCOUS MEMBRANE OF RATS EXPOSED TO COLD

B Gušić, Z Krajina, J Lakić, V Konić and I Babić
Zagreb, Yugoslavia

From the Otorhinolaryngological Clinic (Prof Dr B Gušić) and from the Pediatric Clinic (Prof Dr P Erak) of the Medical Faculty, University of Zagreb

Thirty five albino rats were exposed to low temperature between 0°C and −18°C below zero during a period between 7 and 30 days Bacteriological and histological analyses of the respiratory mucous membrane of the rats were made

Cold leads to the decrease of the temperature of the nose either indirectly by the cooling of the skin or directly affecting the nasal mucous membrane itself Indirect influence takes place reflexively through the sympathetic nerve and the reaction depends also on constitutional characteristics of the organism Direct effect of the cold upon the nasal mucous membrane leads

TABLE 1

Groups	No of animals	Temperature duration of exposition	Richness of growth	Potentially pathogenic flora	Saprophytic flora	Sterile
A B C	15	At 0 and 18 C below 0 7 to 17 days 24 hours daily	+ + +	8	11	4
D E F$_1$	15	At 18 C below 0 18 to 30 days 6 hours daily	+ + and +	1	4	11
N	10	Control group not exposed to cold	+ + +	3	1	7

+, From 1 to 100 colonies + + From 100 to 1000 colonies + + + 1000 or more colonies

Potentially pathogenic flora
Streptococcus haemolyticus
Staphylococcus pyogenes aureus
B proteus E coli Enterococcus

Saprophytic flora
Streptococcus viridans
Streptococcus anhaemolyticus
Staphylococcus albus and aureus coagulase neg.
Dyphtheroid Saproph Neisseria
Saproph cocci Antracoides



Fig 3

chose the albino rats We kept the first group of five rats for seven days and the second group for 17 days continually

After having endured the temperature of 0°C a further group of animals were kept for seven days at the temperature of 18°C below 0 and then for eight hours daily further groups from 18 to 30 days A separate group of five rats kept at the temperature of 40°C below zero died the first night The control group consisted of ten rats We used a total of 45 rats

We took the bacteriological smears before putting them into cold rooms and immediately after their death and made a histological analysis of the mucous membrane of the nose and the trachea

RESULTS

Bacteriological Findings

As can be seen from the enclosed table of the findings the investigations have given the following results With the animals that were exposed continually to 0°C or 18°C below 0 for 24 hours in the course of seven to 17 days

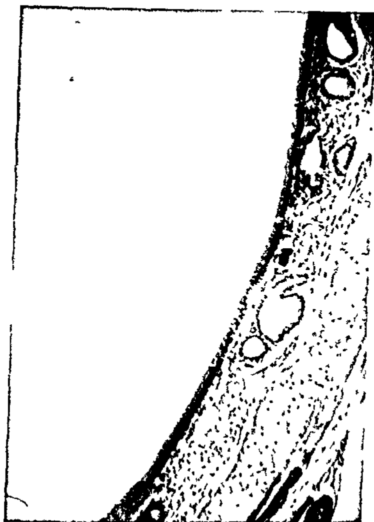


Fig 2

It is possible that all the changes within the nasal mucous membrane are actually a kind of adaptation to the changed conditions of the external surroundings, adaptation to the new conditions of circulation and the decreased consumption of oxygen It is difficult to say when this adaptation will turn into an irreversible state because this depends not only on the quantity and the quality of the excitation but also on the power of adaptation of the nasal mucous membrane This adaptation must also be within the frame of the general functions of the organism, because it is known that longer exposition to cold also causes the hypofunction of the endocrine glands due to the spasms and the consecutive stagnation

We posed ourselves the following questions What is the effect of the continual cold upon the nasal mucous membrane and what of a temporary influence of cold of eight hours within 24 hours through a shorter or longer period of time? What are the repercussions on the lower respiratory tracts? What is the behaviour of the bacterial flora on the nasal mucous membrane? We chose the temperature of 0, 18 and 40°C below 0, which temperatures are available in our refrigerators, and for the experimental animals we



FIG 5

Nose Initial changes of epithelium in the shape of the formation of goblet cells and oedema of the mucous membrane *Trachea* Infiltration of lympho cytes of the subepithelian layer with oedema Superficial epithelium pre served

Group B (five rats temperature of 0°C 10 days 24 hours daily) *Nose* Multiplied goblet cells of the superficial epithelium as well as the glands with large mucous cells and enlarged outleading canals *Trachea* Deficient superficial epithelium with accumulations of lymphocytes

Group C (Fig 5) (five rats temperature of 0°C 17 days 24 hours daily) *Nose* Strong metaplasia of the respiratory epithelium into a multistratified and squamose one which descends deep into the glands Multiplied fibrous tissue with the infiltration of lymphocytes and plasma cells and the restricted amount of leucocytes *Trachea* Deficient superficial epithelium with larger accumulation of lymphocytes at the bottom

Group D (five rats temperature of 18°C below 0°C 18 days 8 hours daily) *Nose* Respiratory epithelium with multiplied goblet cells and very pronounced



Fig 4

the richness of the potentially pathogenic as well as saprophytic flora was more considerable than with the group of animals exposed to a cold of 18°C below 0 for eight hours daily through the period of 18 to 30 days While in the first group of 15 animals there were only four sterile smears in the second group of 15 examined animals there were 11 sterile findings and only in one case potentially pathogenic flora was found In the first group potentially pathogenic bacteria were found in eight animals Also a greater number of sterile specimen was found with the animals which were exposed to the same temperature but for a shorter time

In the control group of 10 animals seven had sterile smears while with three animals potentially pathogenic and saprophytic bacteria were found

Histological Findings

Normal mucous *membrane of the nose and trachea of the rat (Figs 1, 2)*

Group A (Figs 3 4) (five rats temperature of 0°C 7 days 24 hours daily)

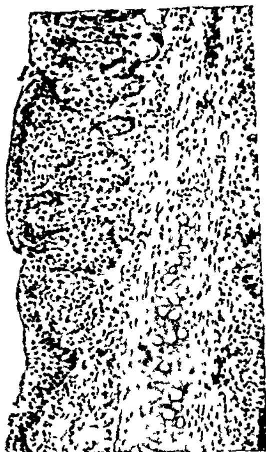


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Group D (five rats temperature of 18°C below 0°C 18 days 8 hours daily) *Nose* Respiratory epithelium with multiplied goblet cells and very pronounced

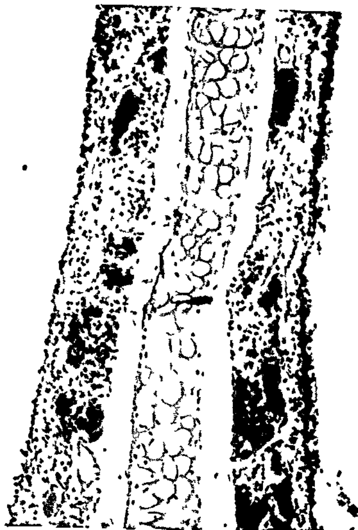


Fig. 6

hyperemia of blood vessels subepithelially. *Trachea*. Changes of epithelium resulting in the peeling and the formation of goblet cells. Subepithelially an oedema.

Group E (Fig. 6) (five rats, temperature of 18°C below 0 6 days 8 hours daily and of 40°C below zero 24 hours). *Nose*. Deficient respiratory epithelium. Non characteristic form of glands (epithelial cells of the glands are peeled off into the lumen, without secretion and with considerably degenerative changes). *Trachea*. Deficient epithelium with a strong inflammatory infiltration and necrosis.

Group Γ (Figs. 7, 8) (ten rats, temperature of 18°C below 0 30 days eight hours daily). *Nose*. Decreased number of cylindrical ciliary cells and multiplied goblet cells and subepithelial glands. Multiplied fibrous tissue with inflammatory infiltration. *Trachea*. Deficient epithelium with a very pronounced suppurative inflammation. Suppurative matter in the lumen.

Larynx. In all groups slight changes on the mucous membrane of the larynx, except group Γ with a pronounced inflammatory infiltration.



Fig 7

Surrenal gland, Group B In all the layers of the cortex there are quite a number of sudanophil grains and a few empty vacuoles

Group F There are no sudanophil grains in any layer of the cortex and there are many empty vacuoles

COMMENT

Our bacteriological and histological investigations have proved that the damage of the nasal mucous membrane of rats exposed to cold takes place oftener and sooner with the continual exposure to cold Histological changes take place within the scope of already known changes as well as with all exogenic or endogenic noxae on the respiratory mucous membrane in the beginning the increase of goblet cells and gland elements, later on, their disappearance together with metaplasia of epithelium and the increase of the fibrous tissue as a final result of inflammatory and degenerative changes Exposure to cold of one month even in intervals of eight hours daily, does



Fig 8

not lead to serious bacteriological or histological changes on the nasal mucous membrane, but has stronger repercussion upon the mucous membrane of the larynx and trachea We can suppose that biological damage of the nasal mucous membrane without as yet visible histological final changes can evidently influence the function of the nasal mucous membrane thus leading to repercussions upon the lower respiratory tracts A prolonged stress of cold can also lead to changes of endocrine glands, as with our rats of the surrenal glands, which can indirectly produce a stronger damage of the respiratory mucous membrane

RÉSUMÉ

35 rats albinos furent exposés au froid entre 0° et −18°C pendant une periode de 7 à 30 jours Des analyses bactériologiques et histologiques de la muqueuse respiratoire des rats furent faites

ZUSAMMENFASSUNG

35 Albinoratten wurden in einem Zeitraum von 7 Tagen bis zu einem Monat einer Kälte von 0°C bis −18°C ausgesetzt Es werden die bakteriologischen Befunde und die histologischen Bilder dieser Respirationsschleimhaut besprochen

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Otorhinolaryngological Clinic Medical Faculty
Zagreb Yugoslavia

DISCUSSION

E Huizinga Cold has been a great problem for a very long time It is already in the word that people expect a relation between cold temperature and to get a cold Still the generation of my teachers did not believe in this relation This relation was proved in Germany during World War I, in the U S A and in Holland by the good researchwork of M Loghem At the other side it is proved that a cold is the result of a virus infection Probably there are different factors The whole problem is very difficult Patients operated with hibernisation don t get a cold

This paper is very important because it was demonstrated that serious lesions of the mucous nasal membrane are caused by cold Are they also found in human beings? That would be a good explanation of this relation

Z Krajina (Reply) We made these experiments because in our refrigerators many workers have very often common cold inflammations of the lower respiratory tract and of the urogenital tract In this way we can now better understand the clinical observations We used in our experiments the same temperatures in which the workers do their work

TIME LAPSE RELATION TO CHANGES IN THE RESPIRATORY EPITHELIUM AFTER MINIMAL TRAUMA[1]

A. C. Hilding
Research Laboratory, St. Luke's Hospital
Duluth, Minnesota, U.S.A.

(1) A series of changes takes place in the respiratory epithelium in extirpated cow tracheas after a light swab has been passed over the surface. These take place over a period of 1 to 24 hours and are characterized by progressive loosening from one another of the columnar cells and cleavage from the underlying cells with subsequent loss of cell form and complete exfoliation of the columnar layer. A new surface forms on the remaining cells giving the appearance of a thin flat epithelium. (2) During these changes the epithelium becomes progressively more fragile and even after just two hours can usually be wiped away cleanly with a 5 gram swab. (3) The staining of the cells by methylene blue seems to be due to injury of the cell and is not dependent upon the presence or absence of overlying mucus. (4) No definite regeneration of epithelium could be determined in the extirpated tracheas even up to 72 hours, although there were suggestions of it.

Trauma to respiratory epithelium and its subsequent regeneration have been reported in many studies. Most of these have dealt with complete destruction of all layers of the epithelium (often including the tunica propria) by incision (Correll & Beattie 1956), excision (Garschin 1935-36), curettage (Wilhelm 1953), foreign bodies (Greenberg & Willms 1962), silver nitrate sticks (Sanderud 1958, Adams & Livingston 1930), formalin (Otto 1957, Burian 1960), toxic gases (Otto & Wagner 1956), tobacco tars (Ross & Kraus 1961), vitamin A deficiency (Wilhelm 1954), methyl cholanthrene (Rigdon & McAnelly 1961) or other equally (from the standpoint of microscopic epithelium) violent methods. Few attempts seem to have been made to produce and study *minimal* trauma and regeneration involving only the superficial layer of columnar ciliated cells. The studies being reported in this paper have to do with this type of minimal trauma.

Last year I reported a series of changes in the respiratory epithelium after such minimal trauma as might occur from the passage of cotton swabs (Fig. 1) across the epithelial surface or the introduction of intratracheal anesthesia tubes (Hilding & Hilding 1962). The results were definite and striking but not always consistent. Many of the specimens taken from the extirpated tracheas of beef animals showed similar and striking changes but

[1] Work supported by Public Health Service Grant No. GM 09603-0, National Institutes of Health.



Fig 1 Cotton swab with adjustable weight which varied the pressure as desired In the current experiments it was adjusted to deliver 10 grams

some mysteriously, showed little or nothing I made another series of experiments in which I carefully controlled each simple step, making each one with my own hands, from the time the workman on the killing floor of the packing plant handed me the freshly excised, intact trachea until the fixed block was safely imbedded in paraffin The swabs were passed within 15 to 30 minutes after the death of the animal and the specimens immediately placed into a mixture of formalin and alcohol Results were largely negative and the changes, which we had come to think of as 'typical' (Fig 2*D*), did not appear at all Even with the heavier swabs, up to 100 grams, these 'typical' findings were absent Lesions resulted, but they were of a different type as from crushing

Fragility

Almost by chance one day I found in one of these unfixed specimens, that in contrast to the untouched epithelium, the epithelium over which the swab had passed became exceedingly fragile This did not occur at once but required some time to develop—sometimes several hours

A series of 42 tests on specimens from the tracheas of 12 beef animals was made to study this phenomenon Cotton swabs, weighted to deliver 5, 10, 25, 50 and 100 grams were passed once over the epithelial surface and stained with methylene blue To test fragility, a swab delivering only 5 grams was passed at right angles across the blue stained track in each If the swab were passed immediately, or any time in the first hour after making the track *the blue* stained track did not wipe away at all But, if the specimen had been lying in a plastic bag at room temperature for 2 or 3 hours, the nly with a 5 gram swab The blue material that



FIG 2 *A*

FIG 2 Changes taking place in the epithelium of a single extirpated trachea of a freshly killed cow after one passage of a cotton swab delivering 10 grams of weight The resulting track in this experiment was not stained The specimens were kept in a moist plastic bag at room temperature after the passage of the swab until dropped into a fixative of alcohol formalin at intervals of time (*A* Immediately after passage of the swab *B*, after 1 hour *C*, *D*, *E*, and *F*, after 2 4 7½ and 24 hours respectively) *A*, The cilia are gone and the end plates appear disrupted *B* The columnar cells are separating from one another and spilling out part of their cytoplasm at the surface *C*, There is a definite line of cleavage through the epithelium under the columnar cells A secondary surface is forming over the replacement cells The layer of columnar cells has shortened and the nuclei appear pyknotic *D* A continuation of the changes in *C* *E*, The layer of columnar cells is holding on only by some of the tail like processes Some of the cells are no longer recognizable and there are some naked nuclei *F* After 24 hours only a few columnar cells remain and a smooth surface has formed over the remaining layers In some specimens the layer of columnar cells had disappeared in 12 hours *G*, Appearance of undisturbed epithelium beside the track after 24 hours

came away upon the swab, when put under the microscope, proved to be a mass of blue stained epithelial cells and not mucin

Previous experiments had demonstrated that no obvious postmortem change takes place in healthy respiratory epithelium kept at room temperature, in less than 24 or 48 hours (Fig 2*G*) Because of this, postmortem changes in the damaged epithelium had not been considered But, this development of fragility in epithelium over which a swab had passed, raised another possibility In fact, it became apparent that the time lapse between the passage of the swab and the time of fixation was the key to the development of the "typical" changes that had been previously reported and which I had not been able to reproduce

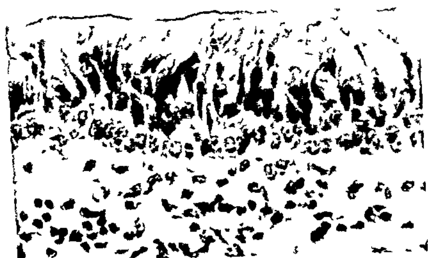


Fig 2 *B*



Fig 2 C

It was found further that the longer the passage of the initial swab after the death ... orter the period required for fragility to ... ept for 6½ hours at room temperature and ... ined blue the fragility became apparent



Fig. 2D

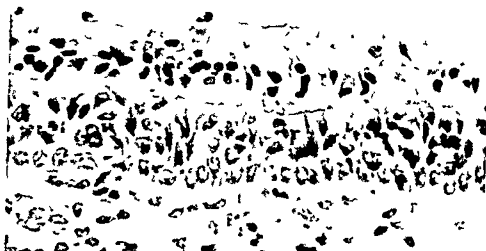


Fig. 2E

Effect of Time lapse

A new set of experiments was designed to test the effect of time lapse upon the histologic appearance of the wounded epithelium

Methods and Materials

The tracheas of 17 freshly killed cows were excised within a matter of minutes and were cut into eight or ten pieces 6 to 8 cm in length The two



Fig 2 F



Fig 2 G

end pieces were discarded because of the possibility of damage from the workmen s fingers

A cotton swab 3 mm in diameter wound on a 15 cm wooden applicator was weighted with an adjustable leaden weight in such a way as to deliver a pressure of 10 grams at the wound end when held horizontally by a thread

at the other end (Fig. 1). Such a swab was passed once along the ventral midline of each piece of trachea, using a fresh swab for each piece. This was done at the packing plant within 30 minutes of the death of the animal. Each swab track was then stained with methylene blue for 1 to 3 minutes and washed with 0.9 % saline. (The swab tracks all stained a deep blue in contrast to the adjacent epithelium. The blue stain of the swab tracks made in extirpated tracheas remained largely unchanged for many hours—even up to 12 to 24 hours.)

One of the pieces of trachea was then immediately fixed in a solution of formalin one part and 80 % ethyl alcohol nine parts, the other pieces were put into a moist plastic bag and carried to the laboratory, where they were kept at room temperature. At intervals up to 24 hours (and, in a few instances, more—up to 72 hours) additional pieces of trachea were similarly fixed. From many of these, a small sample was first cut and examined for ciliary action under the Greenough microscope. If ciliary action is present it can readily be seen by looking carefully in the highlights reflected from the mucinous surface (Proetz, 1953).

After fixation for at least 24 hours, a small block was cut from each piece of trachea, dehydrated, imbedded in paraffin, sectioned, and stained with hematoxylin eosin. The blocks were cut and trimmed in such a way as to place the track in the middle. As stated, no hands but my own handled the tissue until after it was imbedded in paraffin, and all contact with the epithelial surface, from whatever source, was carefully avoided. Much of the cartilage was cut away from each block before dehydration. Each block was manipulated by means of sharp ophthalmic scleral fixation forceps and grasped only upon the cartilage. I am certain that the epithelial surface of any of the retained blocks was not accidentally grasped or bumped or injured in any other way than by the passage of the swab. If, during the preparation of a block, slippage occurred that might have caused some contact with the epithelium, that block was discarded.

Results—Microscopic Findings

The effect of a time lapse between the passage of the swab and fixation was unexpected and marked (Fig. 2). It explained the inconsistencies encountered in previous experiments. When fixation was immediate, the demonstrable damage was *slight*. *In these experiments, using only a 10 gram swab*, the immediate evidence of damage was so slight in some specimens that the location of the track could be determined with certainty only by measurement. In most, there was loss of cilia in the region of the swab track, with slight roughening of the surface, where the end plates of the cells seemed torn and separated from adjacent cells. Some sections showed a degree of separation of the columnar cells for much of their length.

When 1 hour intervened between swabbing and fixation, the separation of the columnar cells from one another was marked, beginning separation

from the underlying cells began to appear, and the surface was ragged By 2 hours the nuclei seemed pyknotic, the columnar cells more separated and a definite line of cleavage between the columnar and replacement cells was apparent About this time a definite, new surface line appeared upon these replacement cells which remained attached to the basement membrane As the time between injury and fixation increased the degree of the changes also became greater The separation of the layer of damaged columnar from the underlying cells increased and it could be seen that the former were holding on only by some of the thread like processes extending down to the basement membrane These intact tail like processes became progressively fewer and the secondary surface more smooth as the time lapse became greater Also the columnar cells continued to separate from one another and to lose their characteristic morphology more and more The nuclei became pyknotic and the cytoplasm and cell membranes disintegrated to the point after some 6 hours where the cells were no longer recognizable and many of the nuclei were lying free and naked By 12 hours many of the columnar cells were entirely gone After 24 hours almost none remained, and the replacement cells formed a smoothly surfaced layer from one to three or four cells deep This remaining epithelium appeared almost metaplastic and in some areas in some specimens looked as though it might possibly be regenerating (Fig 2A F)

Most of the small fresh samples removed just prior to fixation of the various pieces exhibited ciliary action on both sides of the swab track but no ciliary action was found in any of the tracks Even if they had not been stained most of the tracks could have been identified by the lack of ciliary action

Meanwhile the undamaged epithelium just half a millimeter away from the track margin remained unchanged for more than 24 hours (Fig 2G) In fact the postmortem changes in the undamaged epithelium not fixed until after 72 hours were slight

In all of these experiments ciliary action continued in the regions of unmolested epithelium but in none was any ciliary action found where the swabs had passed

Effect of Mucous Blanket and of Dye

It struck me that possibly the swab tracks stained because the *mucous blanket had been removed* Also the thought occurred to me that *it might be the methylene blue* that was making the observed changes I wondered *further if the swabs* would do as much damage if they were *thoroughly covered with mucus*

With these thoughts *in mind* a few further experiments were carried out

Methods

A small series of experiments was done in which the swabs were passed transversely in the *trachea* *In these* experiments the tracheas of six animals

were split along the dorsal midline and spread flat by nailing to a board. The swabs were then passed transversely across the mucous membrane and the tracks not stained at once. Instead, small amounts of India ink were placed on the mucosa upstream (in the ciliary stream) from the swab tracks. Time was allowed for the ciliary stream to carry the ink and mucous blanket well past the line of the swab track, thus insuring that the latter was again covered with a continuous mucous blanket. Then methylene blue was applied as in the other experiments.

In another small series (three animals) swab tracks were made as just described except that they were not stained. They were examined under the Greenough microscope for ciliary action and then the supposed position of the tracks marked with pins. A small sample was removed before fixation and stained to check the correctness of the supposed position of the tracks.

In some other studies relating to chemistry 10 gram swabs were passed repeatedly for a distance of some 200 mm along the anterior surface of a series of five tracheas so that the effect of loading with mucus could be observed.

Results

The transverse swab tracks that were re-covered with mucus stained as promptly and deeply as the longitudinal ones that were stained immediately without making any attempt to see that they were covered with a mucous blanket.

In the unstained series the track was correctly identified by lack of ciliary action as confirmed by staining the small samples. The changes in the epithelium in the hours following trauma were similar in all respects to the stained specimens unless the progressive changes might have been less rapid.

In the mucus loading experiment after being dragged along the epithelial surface for 100 to 150 mm the swabs no longer made tracks that stained. When laden with mucus they would slide very easily, perhaps harmlessly over the epithelium.

Serotonin and Fragility

It has been said that fragility of the respiratory epithelium is produced by the liberation of serotonin (Krueger & Smith 1960, Krueger 1962). Preliminary tests were made to see if per chance serotonin is involved in these changes that occur after this type of minimal trauma. Experiments were done to determine (1) if serotonin could be found in saline used to flood the traumatized area, (2) if serotonin solution in saline would produce histologically visible lesions in untraumatized, healthy epithelium, (3) if the mucous blanket had an effect on serotonin in a saline solution.

Two experiments in which traumatized epithelium was flooded with saline for 5 hours were done in the tracheas of freshly excised cow respiratory tracts enclosed in plastic bags. No serotonin was found in the saline when tested by diazotized paranitroaniline.

In two other preparations the tracheas were so arranged that two pools of 5 ml each could be formed one of saline and the other of serotonin dissolved in saline (10 gamma/ml) The pools were allowed to remain for 8 hours At the end of 8 hours, the serotonin pools from the two preparations were aspirated and tested for serotonin by paper chromatography No serotonin was found in one and, in the other, it was greatly reduced Then specimens were taken for histologic examination No definite changes were found in the epithelium These are preliminary experiments only and may have no significance

Tracheas of Living Animals

Experiments on the tracheas of living animals have been begun At this time I can only report on a single animal

Materials and Method

This animal a 4 day old Guernsey male calf was anesthetized by intra venous injection of pentobarbital sodium at the farm where it was born and then transported to the laboratory It was kept asleep for 27 hours by the addition of small amounts of anesthetic given intraperitoneally at intervals of a few hours and was sacrificed at the end of the 27 hours

A tracheotomy was performed low down on the left ventral aspect of the trachea as soon as the animal had been brought to the laboratory, and then the trachea was exposed on the left side for nearly its full length Care was taken to destroy as little of the circulation as possible The trachea was rotated to bring the dorsal midline into view and it was opened along that line after first coagulating all layers with diathermy in order to control all bleeding along the incision Ten gram swabs were passed over the mucous membrane along the ventral midline Three dry swabs were used each covering about one third of the distance The trachea was then sprayed with methylene blue (The track of the swabs stained well)

Six specimens were removed at intervals and placed in alcohol formalin The first was taken as soon as practicable and dropped into the fixative immediately Perhaps 10 to 15 minutes elapsed between the passage of the swabs and the taking of the first specimen The other specimens were taken after intervals of 1 2 4 8 and 24 hours In the interim between taking the specimens the incised skin of the neck was kept closed by skin clips After removal of the 8 hour specimen the skin was sutured and the animal transported back to the farm where it was placed on a blanket in a warm stall It did not awake and at the end of 27 hours (24 hours after making the swab track) was sacrificed by an intravenous injection of a lethal dose of barbiturate sodium and the final 24 hour specimen removed and placed in fixative

Result

In general the changes were similar to those found in the extirpated tracheas excepting that they were greatly accelerated time wise The blue

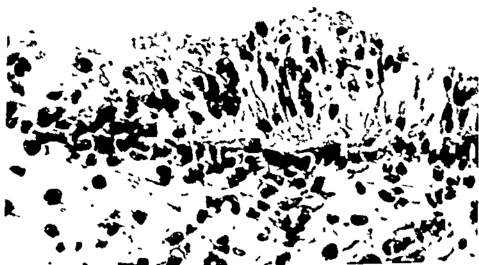


FIG 3 A

FIG 3 Changes in the tracheal epithelium after passage of a 10 gram swab in one living anesthetized animal Specimens A, B, C, and D were taken and fixed respectively 10 minutes, 4, 8 and 24 hours after passage of the swab Already, at the end of 1 hour, the columnar cells had all exfoliated completely a condition reached in the extirpated tracheas only after 12 to 24 hours The 24 hour specimen contains three and four layers of cells in contrast to the 4 and 8 hour specimens which contain only one A number of neutrophils are also present It is of a looser structure than the epithelium in the 24 hour specimens from extirpated tracheas It probably represents regeneration but of this I cannot be sure E, Appearance of undisturbed epithelium at the side of the swab track at the end of 24 hours

stained swab track, instead of remaining clearly evident from 12 to 24 hours, had faded to faintness in 2 hours and was all but invisible at 4 hours

The histologic appearance of the initial damage in the specimen taken immediately was somewhat greater than in most of the extirpated tracheas (Actually 10 to 15 minutes passed before it could be excised in the living animal) Cleavage of the epithelium was advanced at the end of 1 hour and the exfoliating columnar cells were largely gone after 2 hours, and a smooth secondary surface formed over the remaining one or two layers of replacement cells (Fig 3), conditions usually reached in the extirpated tracheas after 12 to 24 hours The 4- and 8 hour specimens were not greatly different than the 2 hour ones The epithelium was one or two layers deep and had a smooth surface

The appearance of the 24 hour specimen was different than anything found in the extirpated tracheas The remaining epithelium was composed of some three layers, which appeared to be very loose and lace like, as though fluid had formed within or between the cells A layer of neutrophilic cells also appeared within the epithelium No mitotic figures were seen (Fig 3D)



Fig 3 *B*

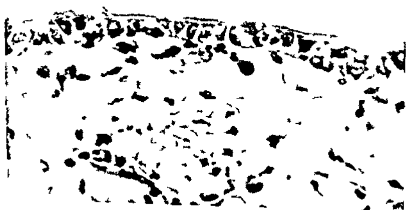


Fig 3 *C*

DISCUSSION

These simple experiments have demonstrated that a series of events culminating in the destruction and loss of the ciliated columnar cells in respiratory epithelium follows in a few hours minimal injury by light cotton swabs in freshly extirpated bovine tracheas. Emphasis is placed on

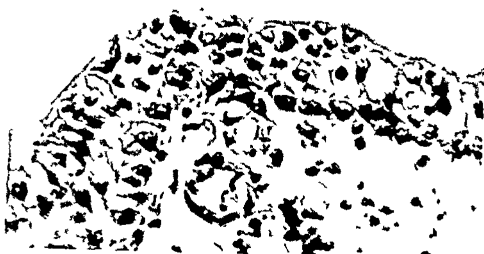


Fig. 3 *D*



Fig. 3 *E*

the fact that these progressive changes occur in the absence *of blood circulation* and in the absence of air flow. The failure of these changes to appear immediately explains my failure to reproduce them in specimens that were placed in fixative promptly. Immediate evidence of the injury can be so minimal that the location of it cannot be demonstrated histologically, with

certainty yet the cells have been mortally wounded so to speak Time is required for the line of cleavage to develop under the layer of columnar cells Additional time is required for these to exfoliate and disintegrate and for a smooth secondary surface to form upon the remaining replacement cells It is of great interest that these progressive changes can take place without circulation in pieces of extirpated trachea lying at room temperature It is also of interest that the fragility observed grossly seems to develop time wise about as the cleavage in the epithelium appears microscopically

The cells that remained attached to the basement membrane might easily under their smooth surface be misinterpreted as metaplastic One may even get the impression in examining these cells after 24 hours that there has actually been regeneration Some of the cells look like very short columnar type with as yet no cilia Such appearances however were usually found near the margins of the track where the trauma might easily have been less severe than in the middle and probably did not represent true regeneration

These changes were not due to postmortem autolysis of normal epithelium because they occurred only where the swab had passed and half a millimeter away the epithelium appeared normal

An impression was entertained that the stain might hasten the changes but in any case the changes found occurred with or without the methylene blue

Neither did the staining depend upon the absence of mucus on the swab track because the transverse swab tracks stained equally well after they had once more been covered over with the mucous blanket

However the damage to cells as indicated by staining did seem to depend upon more or less intimate contact between the swabs and the surface of the cells When the swabs became laden with mucus after having been dragged for 100 to 150 mm they slid over the surface without making a track that stained Apparently if the mucous blanket is not penetrated the swab does not make contact with the cells at all but harmlessly slides over them upon the mucus

In a single live animal in which swab experiments were performed the changes were similar to those in the extirpated tracheas except that they were very much more rapid all of the columnar cells having exfoliated by the end of 2 hours Thereafter there was little or no change up to 8 hours At the end of 24 hours a new picture presented itself namely that of a lacey type of epithelium This epithelium was at least three layers deep in contrast to the s [illegible]

Th [illegible]

epi [illegible] seen it This aspect of the study is being continued partly to determine if this is true regeneration

As far as the relation of fragility to serotonin is concerned in the few experiments done there was no indication of such relation

ACKNOWLEDGEMENTS

Grateful acknowledgement is made to the Elliott Packing Company of Duluth for furnishing the slaughtered beef animals used in this study and for providing the facilities where "immediate" experiments could be carried out, before bringing the specimens to the laboratory I am indebted to Springhill Dairy of Duluth for making the live animal available to me and for providing for its transportation and a part of its care pre- and postoperatively. I would also like to acknowledge the technical assistance and willing cooperation of Mrs Paul Filipi, medical technologist, who assisted with the experimental work, in addition to preparation of the histologic material

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Research Laboratory, St Luke s Hospital, Duluth 5, Minn, U S A

DISCUSSION

Sir Negus In carrying out experiments on eels (Anguilla) one has noticed that after the removal of mucus and immersion in 3 4 % saline solution there is an increase of cells, mainly of goblet cell type These cells appear to arise from the basement layer and I should be glad to hear Dr Hilding s opinion on this point and also as to whether there is a common origin of ciliated and goblet cells

It has been observed that in acute rhinitis there is considerable desquamation of superficial epithelium with regeneration within 24 hours is this true?

This extreme sensitivity of surface epithelium makes one wonder whether much injury is inflicted by passage of a bronchoscope, especially if it is of too large a size for the bronchi into which it is passed

F Huizinga I am much impressed by the demonstration of Hilding of the serious lesions of the mucous membrane by only such a small trauma He agrees with Sir Victor that it gives an indication how careful we must be when putting in a bronchoscope At the other side when it is well done, we see so few reactions in our patients that I will continue this work I should like to ask Hilding if he expects the same lesions in human beings after a small trauma

A C Hilding (Reply) Sir Negus asked about the multiple layers of replacement cells It is my impression that they all come from the basal layer It is also my impression that the goblet cell and ciliated cell have a common origin—in fact are the same cell I think the ciliated cell can become a goblet cell and doubt that the reverse happens

We have thought in the past that regeneration occurs within 24 hours, perhaps even after a few hours These experiments do not settle the question They simply indicate that regeneration may be under way at 24 hours but is by no means complete

I think that Dr Huizinga need not hesitate to pass a bronchoscope The damage in these experiments resulted from a shearing force applied to the surface of the cells reaching through the mucous blanket I have done some experiments on the action of smooth metal to be reported later This makes quite a different picture Pressure without shear is much less destructive It takes considerable force to thin the mucous blanket to 6 or 7 microns—the length of the cilia If the cilia remain upright under pressure then the cell is supported on all sides as from non compressible water—even from within the cell— and distortion does not take place and considerable pressure can probably be sustained Pressure from a smooth bronchoscope handled gently would be of such nature I believe the damage from anesthesia tubes is much greater as is the damage from catheters to remove the secretion Studies on this were reported last year

Of course I do not know if the lesion found in the cow would be the same in man

ÉTUDE DES TERMINAISONS NERVEUSES NEURO-VÉGÉTATIVES AU NIVEAU DE LA MUQUEUSE NASALE

P. ARDOUIN et M. MAILLET
Tours, France

Les auteurs ont étudié la muqueuse nasale du chien et du chat par le procédé de coloration fixation au tétraoxyde d'osmium iodure de zinc (méthode de Champy-Maillet).

Cette technique leur a permis de démontrer au niveau du chorion de la muqueuse olfactive la valeur de l'innervation des glandes de Bowman chez les mammifères fortement macrosmatiques (chien).

D'autre part l'étude de l'innervation des vaisseaux érectiles caractéristiques de la muqueuse pituitaire, met en évidence la richesse de l'innervation musculaire de ces vaisseaux ainsi que l'importance du rôle fonctionnel dévolu à l'entothélium vasculaire dans l'hémodynamique des fosses nasales.

Les fosses nasales des Vertébrés, et plus particulièrement les fosses nasales des Mammifères et de l'Homme, issues de la fossette olfactive primitive, se divisent en deux portions qui se distinguent assez rapidement l'une de l'autre par leur spécialisation progressive : *la portion olfactive*, reléguée dans le recessus olfacto-ethmoïdal et *la portion respiratoire*, qui tapisse la région septoturbinale inférieure.

Depuis les travaux anciens de Zuckerkandl et d'Onodi, la membrane muqueuse tapissant chacune de ces deux zones a fait l'objet de recherches très nombreuses chez l'Homme et dans la série animale, à la fois du point de vue *anatomique*, *histologique*, *physiologique*, et plus récemment, *histochimique*. L'Ecole italienne, en particulier, a fourni une très importante contribution dans ce dernier domaine.

En histologie, Georges Dubreuil de Bordeaux et son élève Marie Valette ont réalisé une étude relative aux dispositifs vaso sensoriels observés chez quelques Mammifères. Du point de vue anatomique et expérimental, le Professeur Kelemen a rassemblé des éléments très intéressants dans le cadre de l'anatomie comparée sur les cavités nasales et para-nasales des rongeurs.

Enfin, plus récemment, un de nos membres les plus éminents, Sir Victor Negus, a présenté un certain nombre de travaux remarquables et désormais classiques sur cette importante question et l'an dernier, à la Réunion d'Athènes, il nous a fait une démonstration magistrale de son talent en nous parlant des fonctions du mucus.

Notre travail est une étude histologique un peu spéciale des muqueuses olfactive et pituitaire. Il tire son originalité de la technique utilisée qui est à la fois simple et élective, en ce sens qu'elle permet la coloration spécifique

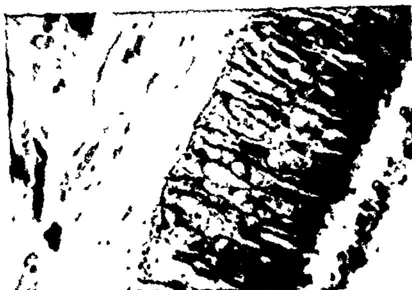


FIG 1 (chien) Épithélium de la muqueuse olfactive du chien Les cellules olfacto-sensorielles se détachent parfaitement (en noir) grace à leur imprégnation par le colorant On distingue 1°) au centre les noyaux de ces cellules (noyaux ovalaires de coloration grisâtre, 2°) la partie supra nucléaire cylindrique et fortement colorée 3°) la partie infra nucleaire plus mince se continuant par l axone de la cellule

des fibres nerveuses amyéliniques du nerf olfactif ainsi que les fibres du contingent neuro végétatif dont l importance est si considerable dans la physiopathologie des fosses nasales

MATERIEL ET METHODE

Technique

Il s agit d un procede de coloration fixation qui differe totalement des méthodes d imprégnation classiques de Golgi de Bielchowsky ou de Bodian C est la methode de Maillet (1959) eleve de Champy

Champy avait deja utilise pour l etude de la muqueuse olfactive d Helix Pomatia l osmium iodure de potassium

Mon collegue et ami Maillet a modifie la technique de Champy et l a rendue plus precise en codifiant strictement certaines regles de la technique

Le colorant fixateur utilise par Maillet est le Tetraoxyde d osmium iodure de zinc

D autre part il est necessaire que les fragments preleves soient le plus mince possible

La temperature optima évolue entre 20 et 25° et la duree de la fixation ne doit pas depasser 24 heures Enfin l epaisseur des coupes doit se situer entre 10 et 15 microns

Ainsi realisees les coupes une fois faites sont pretes a etre lues apres passage au toluene et montage au baume



FIG 2 (chien) Innervation des glandes de Bowman (chorion olfactif) On voit au centre trois glandes de Bowman et leur innervation Au milieu et à gauche une glande de Bowman va être abordée par des fibres nerveuses amyéliniques provenant d un faisceau nerveux sous jacent Ce faisceau est encore ici entouré de sa gaine conjonctive (voir texte) En haut et à droite les fibres commencent à se dégager de leur gaine pour aborder la glande

MATERIEL

Nous avons applique cette methode à l'étude de la muqueuse olfactive et pituitaire du chat, du chien et de l'Homme

Les fragments de muqueuse de chat et de chien ont été prélevées sous anesthesie générale

Chez l'Homme, nous avons pu saisir des fragments analogues au cours de certaines interventions endonasales

RESULTATS

En ce qui concerne les résultats, une premiere constatation s impose, c'est la parfaite mise en evidence *de l epithelium olfactif*

En effet, dans les muqueuses olfactives du chien, du chat et de l Homme, la disposition des cellules olfactives a été remarquablement revelée par le réactif, et la coloration est superposable aux bonnes imprégnations que l on peut parfois réaliser avec la technique de Golgi

La partie *supra nucleaire,* cylindrique et la *touffe des cils olfactifs* sont colorées en noir le noyau se détache lumineusement grâce a la surface ovalaire, grisâtre qu il dessine

La partie infranucleaire de la cellule sensorielle, fine, et de calibre irrégulier, adoptant parfois un parcours sinueux, est bien visible, et tranche sur les cellules de soutien *L axone* est souvent variqueux dans sa partie

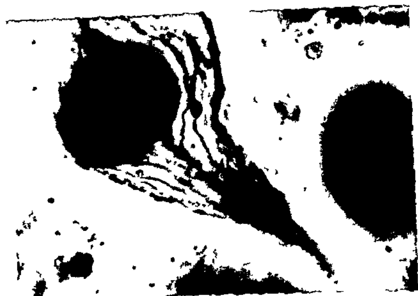


Fig. 3 (chien). Innervation des glandes de Bowman (chorion olfactif). *On a pu dans cette coupe* « surprendre » la phase exacte d'un « encorbellement » d'une glande de Bowman par un pinceau de fibres nerveuses *amyéliniques*.

infra-épithéliale. Ces axones se réunissent à la partie inférieure de l'épithélium *pour* réaliser des *faisceaux* qui s'échappent de proche en proche de l'épithélium.

Les cellules de soutien sont colorées en brun-jaunâtre; on trouve dans la *région supra-nucléaire* de ces cellules des granulations noires; il s'agit de grains de pigment qui ont été surcolorés par le réactif. Ces *grains pigmentaires* ont une structure chimique encore mal définie mais il semble qu'ils contiennent *des substances* lipoïdes puisque, comme l'a démontré récemment Barocci, la méthode de Caccio les colore[1].

La partie du chorion immédiatement sous-épithéliale examinée *après* action du *réactif ne* semble contenir que les faisceaux amyéliniques *qui* forment le *nerf olfactif*: ces faisceaux sont constitués par la réunion de quelques fibres *généralement* très variqueuses: elles contiennent en effet des gouttelettes fortement *colorées en noir* se détachant sur le reste de l'axoplasme lui-même *imprégné en gris*. La méthode de l'osmium-iodure de zinc ne nous a pas révélé l'existence d'autres fibres dans cette région.

Dans la zone profonde *du chorion* nous trouvons des faisceaux plus volumineux formés *par la réunion* des faisceaux précédents: leurs fibres colorées en gris sont de calibre régulier: ces éléments sont séparés les uns des autres par des espaces *conjonctifs* étroits contenant les glandes de Bowman.

[1] Barocci: Vascolarizzazione e struttura dei vasi della mucosa nasale *pars respiratoria* e pars olfattoria. Rassegna internazionale di clinica e terapia 40, 1960, p. 441–451.



FIG. 2 (chien). Innervation des glandes de Bowman (chorion olfactif). On voit au centre trois glandes de Bowman et leur innervation. Au milieu et à gauche une glande de Bowman va être abordée par des fibres nerveuses amyéliniques provenant d'un faisceau nerveux sous-jacent. Ce faisceau est encore ici entouré de sa gaine conjonctive (voir texte). En haut et à droite les fibres commencent à se dégager de leur gaine pour aborder la glande.

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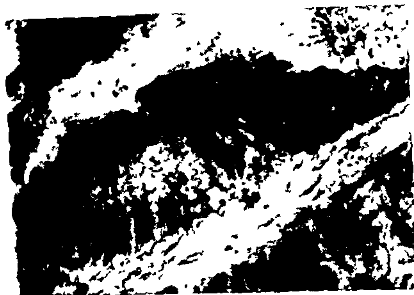


Fig 5 (chat) M n e e n a t h
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vation de chacun des f bres muscula res lisses (voir texte)

Épithélium de la muqueuse pituitaire (chat chien homme)

En ce qui concerne la membrane de Schneider certaines cellules prismatiques ciliees de la muqueuse pituitaire se colorent completement en noir, laissant apparaitre en plus clair la zone réservée au noyau les cils memes des ces cellules sont colorés en noir tandis que leur base offre *souvent un* aspect fourchu ou effilé chaque branche de la fourche enserrant *une cellule basale* terminée par un renflement

Dans la région examinee (muqueuse pituitaire en bordure de la muqueuse olfactive) la couche conjonctive séparant l epithelium des glandes est peu épaisse elle est occupée par des vaisseaux accompagnes de leur contingent habituel de fibres amyéliniques De ces faisceaux partent quelques fibres fines moniliformes qui pénètrent dans l epithelium et cheminent dans la partie basale de cet epithelium certaines cheminent parallelement a la basale de l epithelium et expedient de courts eléments qui traversent cette basale perpendiculairement Cette innervation est totalement independante de celle des glandes du tissu erectile ces fibres se terminent par des extrémites renflees en bouton au contact des cellules basales

Les vaisseaux érectiles

Nous les avons surtout examinés chez le chat

Les vaisseaux érectiles de la muqueuse pituitaire du chat recoivent une innervation particulierement riche Les fibres amyéliniques de nature sym



FIG. 4 (chat). Muqueuse pituitaire du chat — face profonde du chorion. Cette coupe vue à un fort grossissement dégage deux vaisseaux érectiles et montre bien l'importance de l'endothélium vasculaire dont on peut apprécier l'épaisseur. Elle permet de vérifier la disposition du corps musculaire constitué par des fibres lisses ainsi que le développement de l'innervation qui s'y rapporte. Noter également le comportement de certaines fibres nerveuses amyéliniques qui traversent les fibres musculaires pour se diriger vers les cellules endothéliales.

Innervation des glandes

L'innervation des glandes se présente d'une manière différente dans les trois espèces étudiées. L'innervation des glandes de Bowman du chien est la plus riche.

Ainsi chez le chien les glandes de Bowman sont abordées par un ou plusieurs faisceaux de fibres amyéliniques; ces faisceaux groupent un grand nombre de fibres. Ils sont en général entourés par une gaine conjonctive mais ceci n'est pas obligatoire. Arrivées au voisinage de la glande, il est fréquent de constater que les fibres s'écartent et contournent la glande de part et d'autre. Certaines de ces fibres cheminent entre la membrane basale de l'épithélium glandulaire et abandonnent des ramifications courtes qui vont se terminer entre les cellules glandulaires.

Chez le chien nous avons également observé des nerfs mixtes curieux avec séparation des fibres nerveuses amyéliniques et myélinisées; ces nerfs sont entourés par leur gaine conjonctive et on note la présence d'une cloison médiane fine déterminant dans la gaine commune deux compartiments, l'un pour les fibres amyéliniques, l'autre pour les fibres myélinisées. La destination de ces nerfs nous est inconnue.

Chez l'Homme, mammifère microsmatique, ce dispositif est encore plus sommaire.

Ce problème nous paraît suffisamment important pour justifier des recherches ultérieures.

Nous avons pu également démontrer toute la valeur de l'innervation des glandes de Bowman chez les Mammifères macrosmatiques, indiquant ainsi le rôle adjuvant très appréciable joué par cet appareil glandulaire dans l'ensemble des processus, encore mal éclaircis, de la physiologie de l'olfaction.

Enfin, en ce qui concerne la muqueuse pituitaire, il nous a été possible, non seulement de mettre en évidence l'individualité de l'innervation respective de chaque fibre musculaire lisse des vaisseaux érectiles, mais surtout, de dégager l'importance du rôle fonctionnel dévolu à l'endothélium vasculaire, comme le prouvent les relations de contact intime établies entre les terminaisons nerveuses amyéliniques et le cytoplasme des cellules endothéliales.

SUMMARY

The authors have investigated the nasal mucous membrane in dogs and cats, by Champy's and Maillet's method (osmium tetra oxyd and zinc iodure).

This proceeding has enabled us to demonstrate in olfactory mucous membrane the value of the innervation of the Bowman's glands observed in macrosmatic mammals (dog).

On the other hand in pituitary mucous membrane, the investigation of the erectile vessels points to the value of the muscular innervation, and brings out the importance of the functional part of vascular endothelium in the hemodynamism of the nasal mucous membrane.

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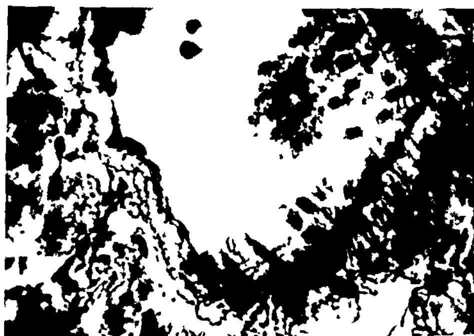


FIG. 6 (chat). Muqueuse pituitaire du chat — innervation de la paroi endothéliovasculaire. Cette coupe a été prise tangentiellement, ce qui a permis de dégager un nombre très important de cellules endothéliales. On voit parfaitement ces cellules se détacher dans la lumière du vaisseau et on peut distinguer la richesse de l'innervation qu'elles reçoivent de la part des fibres nerveuses amyéliniques qui cheminent à travers la paroi musculaire.

pathique qui la constituent sont extrêmement sinueuses, très variqueuses, possédant de très nombreuses ramifications. Ces fibres sont si nombreuses qu'il semble bien que chaque fibre musculaire lisse soit innervée (voir fig. 5).

L'endothélium des vaisseaux érectiles est fortement coloré en noir; il est remarquable de constater que cet endothélium reçoit une innervation dépendant des ramifications qui s'échappent des fibres amyéliniques de la musculeuse.

Les glandes séreuses de cette région reçoivent une innervation très discrète, moins importante qu'au niveau de la muqueuse olfactive. Il s'agit de fibres amyéliniques qui semblent dépendre du plexus périvasculaire.

CONCLUSION

Nos recherches nous ont permis tout d'abord de mettre en lumière les divers constituants de la muqueuse olfactive et plus particulièrement au niveau des cellules de soutien de dégager les granulations pigmentaires, anciennement étudiées par Lister chez les Vertébrés inférieurs et interprétée depuis par Sir Victor Negus comme favorisant les sensations olfactives en relation avec la fonction visuelle.

A ce sujet, nous devons signaler que MM. Philippot et Gerebtzoff de l'Université de Liège, étudiant la nature du pigment olfactif, concluent à la bipolarité électrique de ses constituants, argument qu'ils portent à l'actif de la théorie électro-statique de l'olfaction.

THE QUANTITATIVE VALUES OF MUCIN IN RESPIRATORY TRACT IN NORMAL AND PATHOLOGICAL CONDITIONS

M Pražić and K Weber
Zagreb, Yugoslavia

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There were only patients with quite normal nasal status. We measured the mucin from both sides of the nasal cavity twice. The second measuring was performed with all patients 2 hours after the first measuring. Our measurements have shown that in quite normal conditions the quantity of mucin in nasal mucus varies very widely in the values from 1–4.

We performed measurements of mucin in nasal mucus with patients with different pathologic findings. With a patient who had fractura inveterata dorsi et septi nasi the left side of the nasal cavity was narrowed and the breathing through this side was reduced. The measuring of mucin in nasal mucus gave the following results:

Right	Left
2 017	0 59[illegible]
2 674	0 800

The values of mucin in the left, obstructed side are very low.

A patient with a severe rhinocyphosis could not breathe through the nose. Our measuring of mucin gave the following results:

Right	Left
0 870	0 603
0 9 6	0 394

The values of mucin are here on both sides very low. We performed many measurements of mucin in patients with Rhinitis vasomotoria in relatively quiet stages as in attacks of profuse secretion.

	Right	Left
Patient No 1	2 217	1 165
	2 680	1 195
Patient No 2	3 180	1 080
	2 165	1 809

With both patients the measurement was performed in a relatively quiet stage and the values are in the range of normal individual variations.

	Right	Left
Patient No 3	0 666	0 503
	0 472	0 851

With this patient the measurement was performed during an attack of profuse secretion and the values of mucin are here very low in spite of profuse secretion.

With the patients with Rhinitis atrophica we received the following results:

	Right	Left
Patient No 1	0 691	0 [illegible]31
	0 620	0 486
Patient No 2	1 460	0 965
	1 160	0 814

the intensity of the band of rays of light which proceeds from the turbid liquid

Mucin is soluble in potassium hydroxide and it is insoluble in neutral or slightly acid solutions At this fact we elaborated our method of turbidimetric determination of the quantitative values of mucin in the mucus

If we take the mucus which contains mucin in the solution of potassium hydroxid this solution will dissolve the mucin Remaining insoluble substances and particles we put away by filtration If we give now to this solution a certain quantity of the acetic acid the solution will become turbid because mucin will be transformed into fine particles This turbid solution we measure with the turbidimetry

With this procedure we shall get an extinction which is a relative value for the concentration of mucin in mucus and with it we can state the absolute quantity of mucin by the equation $M = E/T$ M is mucin number and it is the real quantity of mucin E is extinction which is measured with the band of light of 400 millimicrons The diameter of the glass cuvette which contains the solution must be 0 5 cm T is the real weight of mucus For our investigations we choose the mucus from the nose and the procedure of the method is as follows

A tampon of cotton wool which is weighed on the torsion scale we put in the nasal cavity for 10 minutes After 10 minutes we take the tampon out we measure it again on the torsion scale and then put it in the solution of potassium hydroxide To this solution we add certain quantity of the acetic acid and the mucin will be transformed into white fine particles This turbidity we measure by the turbidimetry

In our investigations we wished to answer the question Is the production of mucin in the nasal mucus with all people equal and constant?

We performed about 500 measurements and the results gave us the following conclusions The quantity of mucin in the nasal mucus varies permanently with the same person during the whole day in a rather wide range The quantity of mucin in the nasal mucus of the same person is not the same in both nasal cavities and the variations are rather wide

For the illustrations of these facts there are some results of our measurements of mucin of nasal mucus from both right and left sides of the nasal cavity

	Right	Left
Patient No 1	2 217	1 165
	2 680	1 135
Patient No 2	1 186	1 431
	1 048	1 6[illegible]
Patient No 3	2 438	1 155
	1 130	1 964
Patient No 4	1 975	1 417
	1 621	1 433
Patient No 5	3 508	1 333
	2 085	3 315

Patient No 2	6 a m	1 212	4 p m	4 [illegible]43
	8 a m	2 493	6 p m	4 179
	10 a m	3 387	8 p m	3 460
	12 a m	3 014	10 p m	1 674
	2 p m	5 460	11 p m	0 840

Patient No 2 awoke at 6 a m and we immediately performed our first measurement which gave rather low value After our last measuring at 11 p m which gave very low value of mucin the patient went to bed

CONCLUSION

We elaborated a method for quantitative measuring of mucin in the mucus With this method it is possible to state even the slightest variations of the quantity of mucin in the mucus Although we are in the beginning of our measurements and investigations we could state that the secretion of mucin is a very complex process with a very wide range of variations of the quantitative values of mucin not only with different people but also with the same person during the day even in both sides of nasal cavity

We have ascertained that the quantities of mucin in mucus in patients suffering from severe attacks of rhinitis vasomotoria and in patients with rhinitis atrophica are remarkebly lowered

We state further that for normal secretion of mucus in the nasal cavity and for normal quantities of mucin in mucus a normal respiration through the nose must be regulated If the respiration through the nose is either stopped or disturbed the values of mucin will be lowered

Concerning the problem of snoring we mentioned a new fact the abrupt lowering of the quantities of mucin in nasal mucus before falling asleep and just after awakening

RÉSUMÉ

Par une méthode developpée pour la calculation de la mucine l analyse de la secretion nasale a l etat normal et pathologique fut realisé Il fut constaté que plusiers états pathologiques peuvent etre expliqués avec des valeurs de la mucine

ZUSAMMENFASSUNG

Mit einer eigenen Methode fur die quantitative Bestimmung des Muzins wurde die Analyse des Nasensekrets bei normalen und pathologischen Zustanden durchgeführt Es wurde festgestellt dass die Variationen der Werte des Muzins bei manchen pathologischen Zustanden funktionell erklart werden konnen

Prof Dr M Pra ić,
Ilie Martinkovica br 3 I Zagreb Yugoslavia

With the patient No 1 the values of mucin are very low With the patient No 2 the advanced atrophy was on the left side and on the right side the atrophy was rather mild Therefore the values of mucin for the right side are nearly normal

We performed a series of measurements with tracheotomised patients in whom the tracheotomy was performed on account of different indications We wished to state the values of mucin in these patients who do not breathe through the nose The results in all these patients are nearly the same if we take into consideration normal individual variations We shall show the results of some of these measurements In these three patients very low quantities of mucin are evident

Laryngectomy propter Carcinoma laryngis

	Right	Left
Patient No 1	0 316	0 452
	0 354	0 494

Tracheotomy propter Tetanus

	Right	Left
Patient No 2	0 268	0 217
	0 155	0 401

Tracheotomy propter Myastheniam

	Right	Left
Patient No 3	0 250	0 506
	0 348	0 571

Many measurements of mucin we performed with people who are snoring during their sleep in the night Our measurements in this field connected with some other investigations are not finished This time, therefore, we shall give only some results of our measurements

With the people who are snoring during their sleep we performed our measurings of mucin throughout the day from early in the morning till late in the evening every 2 hours We shall bring the results of two patients only from one nasal side because the variations of the quantities of mucin in both sides of the nasal cavity are in the range of normal variations which we see in all other patients

Patient No 1	7 a m	3 725	5 p m	2 191
	9 a m	5 331	7 p m	2 191
	11 a m	3 205	9 p m	1 006
	1 p m	4 017	11 p m	0 829
	3 p m	3 611		

Throughout the whole day from 7 a m up to 7 p m we obtained quite normal values of mucin in the nasal mucus At 9 p m the value of mucin had fallen and at 11 p m just before patient No 1 usually goes to bed we obtained very low value of mucin

ZELLPROLIFERATION UND ZELLWANDERUNG IN DEN TONSILLEN

A. Meyer zum Gottesberge und F. Koburg
Düsseldorf, Deutschland

In der Tonsille des Kaninchens wurde autoradiographisch mit H³-Thymidin die Zellneubildungsrate bestimmt.

1. Es erfolgen Zellteilungen sowohl in den Sekundärfollikeln (Keimzentren, Reaktionszentren) wie im interfollikulären Gewebe.

2. In den Sekundärfollikeln ist im hinteren (kryptenabgewandten) Abschnitt eine sehr rege Zellteilung festzustellen (H³-Index, Prozentzahl der markierten Zellen nach 1 Stunde 35 %, nach 48 Stunden 94 %). In der Lymphozytenkappe des Sekundärfollikels sind nach 1 Stunde 2–4 % der Zellen markiert, nach 48 Stunden etwa die zehnfache Anzahl. Im interfollikulären Gewebe beträgt die Markierung 6–8 %, nach 48 Stunden etwa das Doppelte.

3. Die Silberkorndichte der in den Sekundärfollikeln markierten Zellen ist um ein Mehrfaches schwächer als die der markierten Zellen der übrigen Gewebe.

4. Markierte Lymphozyten tauchen in der Lymphozytenkappe des Sekundärfollikels nach 6 Stunden auf. Nach 24 Stunden finden sich im retikulierten Kryptenepithel und im Kryptenlumen bereits zahlreiche markierte Lymphozyten und nach 48 Stunden sind fast alle Lymphozyten im Kryptenlumen markiert.

Die Tonsillen gehören wie die übrigen lymphatischen Organe zu denjenigen Geweben des Organismus, bei denen die intensiven Forschungen eines Jahrhunderts immer noch viele Fragen hinsichtlich der Funktion sowie der Bedeutung der einzelnen Formelemente offengelassen haben. Es soll im Rahmen dieses Berichtes nur zu einem Aspekt des Tonsillenproblems Stellung genommen werden, nämlich zu Fragen nach den Orten und der Kinetik der Zellproliferationen.

Der Streit, der über die Frage entbrannt ist, ob die hellen Zentren der Sekundärfollikel entsprechend der Flemmingschen Ansicht Keimzentren oder entsprechend der Hellmanschen Auffassung Reaktionszentren sind, ist bis heute nicht entschieden. Auch exakte, die Gewebsdynamik erfassende Methoden haben widersprechende Ergebnisse gebracht. Autoradiographische Untersuchungen von Yoffey und Mitarbeitern mit dem radioaktiven Chromosomenbaustein H³-Thymidin haben zwar ergeben, daß an Mesenteriallymphknoten die hellen Zentren der Sekundärfollikel als Keimzentren aufzufassen sind. Mit der gleichen Methodik kamen jedoch Fliedner und Mitarbeiter für die Milz zu der Auffassung, daß in den hellen Zentren zwar Zellneubildungen erfolgen, daß aber die dort gebildeten Zellen schwerlich als Vorläufer der peripheren Lymphozyten angesehen werden können. Es muß

DISCUSSION

Sir Negus I have been anxious to obtain some idea of the viscosity of mucus its action is said to depend on physical properties, since the molecules of mucin are very long and form a sort of meshwork Could Dr Pražić kindly explain what the figures given were related to?

A C Hilding The nature of the unit of measure was not clear to me Do the figures refer to percentage or mg/ml?

H A L van Dishoeck Does a connection exist between the rhythmic volume changes of the turbinates and the secretion of mucus, which seems to be rhythmic too, varying from one side to the other?

M Pražić (Reply) To Sir Negus We performed only quantitative measurements not regarding qualitative differences To v Dishoeck We have stated so far only the quantitative condition of mucus in both sides of the nose but we cannot answer now what brings them about To Hilding Our values are expressed as *milliliters*

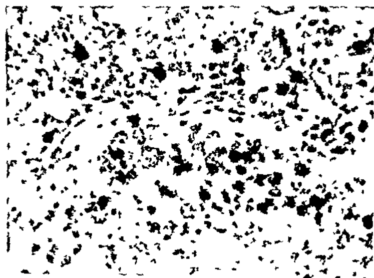


Abb 2 Autoradiogramm des hinteren Follikelanteils und des angrenzenden perifollikularen Gewebes Kaninchen 1 Stunde nach Gabe von H³ Thymidin H E 100fach Zahlreiche schwach markierte Zellen im Rand des Zentrums wenige stark markierte Zellen im perifollikularen Gewebe Die schwachere Markierung der Zellen des Keimzentrums wird dadurch deutlich daß hier viel fach einzelne Silberkorner zu erkennen sind wahrend die markierten Zellen der perifollikularen Zone homogen schwarz erscheinen

Gewebe stammt von einem Kaninchen das eine Stunde nach intravenoser Gabe von H³ Thymidin getotet wurde Die hier durch die schwarzen Silberkorner markierten Zellen waren zur Zeit der Injektion in der DNS Synthese, d h sie stehen unmittelbar vor der Mitose Auf den ersten Blick erkennt man viele markierte Zellen im Epithel und — diffus verteilt — im interfolli kularen Gewebe Bei genauerem Hinsehen fallt jedoch auf, daß in den hellen Zentren die Zahl der markierten Zellen pro Flacheneinheit größer ist Man findet eine deutliche Anhaufung markierter Zellen im hinteren Anteil des hellen Zentrums Der mittlere Teil ist arm an markierten Zellen wahrend innerhalb der Lymphozytenkappe sehr wenige, aber stark markierte Zellen angetroffen werden

In Abbildung 2 ist ein Autoradiogramm des hinteren Follikelanteiles bei starkerer Vergroßerung wiedergegeben Man erkennt bei dieser Vergroßerung deutlicher daß innerhalb des hellen Zentrums etwa viermal so viele Zellen markiert sind wie in dem peri bzw interfollikularen Gewebe In Abbildung 2 wird außerdem deutlich, daß die Intensitat der Markierung d h die Sil berkornzahl pro Zelle starke Unterschiede aufweist Die markierten Zellen im interfollikularen Gewebe und in der Lymphozytenkappe sind stark geschwarzt wahrend diejenigen des hellen Zentrums deutlich weniger Silberkorner haben Dies konnte damit zusammenhangen daß die Zellen des Zentrums auf Grund ungustigerer Gefaßversorgung (Krauspe, Naumann, Fiorelli) weniger Thymidin erhalten, wohingegen den Zellen des interfolli



Abb. 1. Autoradiogramm der Tonsille. Kaninchen 1 Stunde nach Gabe von H³-Thymidin. 100fach. Darstellung der Gewebs- und Zellstrukturen mit Hämatoxylin-Eosin. Die schwarz hervortretenden Zellen sind markiert, d. h. sie haben H³-Thymidin eingebaut. In dem abgebildeten Sekundärfollikel erkennt man zahlreiche markierte Zellen im hinteren Abschnitt des Keimzentrums.

deshalb gleich eingangs darauf hingewiesen werden, daß zwar Ergebnisse, die am Lymphknoten erarbeitet wurden, auf die Tonsillen übertragen werden können, daß dies offenbar aber nur mit großen Einschränkungen für Schlüsse von der Milz auf die Tonsillen gilt. Leider werden die Unterschiede, die zwischen den einzelnen lymphatischen Strukturen existieren, in der Literatur allzu oft übersehen, so daß ungerechtfertigte Analogieschlüsse präsentiert werden.

Die Versuche, über die hier berichtet wird, wurden an Kaninchen ausgeführt. Über die der Versuchsanordnung zugrunde liegenden Überlegungen wurde schon früher berichtet (Meyer zum Gottesberge & Koburg 1962). Sie gehen aus von der Tatsache, daß alle Zellen vor einer bevorstehenden Mitose die DNS ihrer Chromosomen verdoppeln. Mit Hilfe des radioaktiven Chromosomenbausteins H³-Thymidin und der autoradiographischen Technik können daher Orte und Ausmaß von Zellneubildungen verfolgt werden.

Bei der autoradiographischen Methode handelt es sich um eine Kombination von histologischer und photographischer Technik. Die in einem Gewebe inkorporierte Radioaktivität schwärzt die über dem Gewebeschnitt befindliche Photoschicht (vergleiche Plester 1960, Meyer zum Gottesberge 1960, Koburg 1961, Koburg & Plester 1962, Maurer & Koburg).

Im folgenden soll über die mit dieser Methodik an der Tonsille gewonnenen Resultate berichtet werden.

Das in Abbildung 1 wiedergegebene Autoradiogramm stellt eine Übersichtsaufnahme eines Kryptenteiles mit einem Sekundärfollikel dar. Das

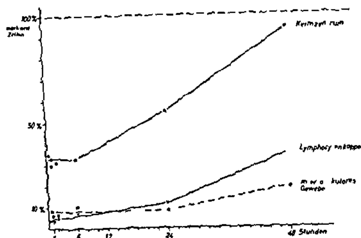


Abb 4 Darstellung des Prozentsatzes markierter Zellen der Tonsillengewebe des Kaninchens nach einmaliger Gabe von H^3 Thymidin als Funktion der Versuchsdauer (Erläuterung im Text)

überein und kann daher in Prozenten ausgedrückt werden Von besonderem *Interesse* ist der H^3 Index bei einer kurzen Versuchsdauer z B bei einer Zeitspanne von 30 Minuten zwischen der Injektion des Tritium Thymidins *und* der Tötung Die bei kurzer Versuchsdauer markierten Zellen stehen *noch vor* der Zellteilung denn erfahrungsgemäß ist die Zeit zwischen dem Ende der DNS Synthese in der das Thymidin eingebaut wird und *dem* sichtbaren Beginn der Mitose länger als 30 Minuten Die bei sehr kurzer *Versuchsdauer* z B 30 60 Minuten nach der Injektion erhaltenen H^3 Indexes geben also den Prozentsatz der teilungsbereiten Zellen *wieder* *Damit* hat man einen Anhaltspunkt für die Berechnung der Generationsdauer der betreffenden *Zellart* *Im Follikelzentrum* sind nach 30 60 Minuten rund 30% der *Zellen markiert* in der Lymphozytenkappe dagegen nur 2–4% Im interfollikularen Gewebe sind etwa 6 8% der Zellen *markiert*

Nach 6 Stunden steigt die Zahl der markierten Zellen im hellen Zentrum an weil sich inzwischen *eine Reihe von Zellen* geteilt hat Auch innerhalb der übrigen Tonsillenanteile der *Lymphozytenkappe* und dem interfolli ku[illegible] verzeichnen [illegible] H^3 Index etwa ve[illegible] nach *weiteren 24 Stunden* also nach insgesamt 48 Stunden ist nahezu eine nochmalige Verdoppelung eingetreten Es sind jetzt nämlich 94% aller Zellen markiert *ohne dass inzwischen* neues H^3 Thymidin injiziert worden wäre

Wie verhalten sich nun die anderen beiden Anteile der Tonsille? Im interfollikulären Gewebe *ist nach 48* Stunden lediglich eine Verdoppelung der Zahl markierter Zellen *erfolgt* Innerhalb der Lymphozytenkappe hat sich jedoch der H^3 Index im Laufe von 48 Stunden verzehnfacht

Zur Interpretation *dieser* Kurven soll vorerst bewußt vereinfacht werden

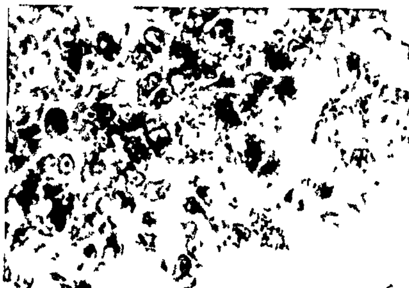


Abb. 3. Autoradiogramm vom seitlichen Rand des Keimzentrums mit Übergang zur Lymphozytenkappe. Kaninchen. H. E. 1000fach. Bei den markierten Zellen handelt es sich um verschiedene Stadien der lymphatischen Reihe. (Erläuterungen im Text.)

kulären Gewebes und der Lymphozytenkappe ähnlich wie den Oberflächenepithelien das Thymidin in höherer Konzentration und über längere Zeit angeboten wird. Andererseits wäre es möglich, daß es sich um verschiedene Zelltypen handelt. Damit wären zellspezifische Unterschiede in der DNS-Syntheserate und damit in der DNS-Synthesedauer (Koburg & Maurer 1962; Koburg 1962) denkbar.

In Abbildung 3 ist ein stark vergrößertes Autoradiogramm eines Teiles des hellen Zentrums sowie des Randes des Lymphozytenwalles eines Sekundärfollikels abgebildet. Man sieht eine markierte große Reticulumzelle. Außerdem sind einige große basophile Stammzellen und Prolymphozyten markiert. Die hier abgebildeten kleinen Lymphozyten der Lymphozytenkappe sind ausnahmslos unmarkiert. Sofern sich, wie in Abbildung 1, markierte Zellen innerhalb des Lymphozytenwalles zeigen, handelt es sich um größere Zellen. Das bedeutet, daß innerhalb der lymphatischen Zellreihe unter normalen Bedingungen nur die großen Vorformen zur DNS-Synthese und damit zur Zellteilung befähigt sind. Dies wird damit bestätigt, daß markierte kleine Lymphozyten erst nach mehr als zwei Stunden auftauchen, also nach einer Zeit, in der sich Zellen geteilt und differenziert haben können.

Es soll nun festgestellt werden, ob sich aus der Zahl der markierten Zellen in Abhängigkeit von der Versuchsdauer Informationen über die Kinetik der Zellproliferation innerhalb der Tonsille ergeben.

In Abbildung 4 ist der H^3-Index als Funktion der Versuchsdauer, d. h. der Zeit nach einer einmaligen Injektion von H^3-Thymidin, graphisch wiedergegeben. Unter dem H^3-Index versteht man den Anteil H^3-markierter Zellen, bezogen auf die Gesamtzahl der Zellen des betreffenden Gewebes. Der H^3-Index stimmt zahlenmäßig mit dem Prozentsatz markierter Zellen

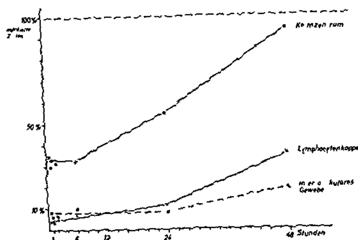


ABB 4 Darstellung des Prozentsatzes markierter Zellen der Tonsillengewebe des Kaninchens nach einmaliger Gabe von H³ Thymidin als Funktion der Versuchsdauer (Erläuterung im Text)

überein und kann daher in Prozenten ausgedrückt werden Von besonderem Interesse ist der H³ Index bei einer kurzen Versuchsdauer z B bei einer Zeitspanne von 30 Minuten zwischen der Injektion des Tritium Thymidins und der Tötung Die bei kurzer Versuchsdauer markierten Zellen stehen *noch vor* der Zellteilung denn erfahrungsgemäß ist die Zeit zwischen dem Ende der DNS Synthese in der das Thymidin eingebaut wird und dem sichtbaren Beginn der Mitose länger als 30 Minuten Die bei sehr kurzer Versuchsdauer z B 30–60 Minuten nach der Injektion erhaltenen H³ Indexes geben also den Prozentsatz der teilungsbereiten Zellen wieder Damit hat man einen Anhaltspunkt für die Berechnung der Generationsdauer der betreffenden Zellart Im Follikelzentrum sind nach 30–60 Minuten rund 30 % der Zellen markiert in der Lymphozytenkappe dagegen nur 2–4 % Im interfollikulären Gewebe sind etwa 6–8 % der Zellen markiert

Nach 6 Stunden steigt die Zahl der *markierten Zellen* im hellen Zentrum an weil sich inzwischen eine Reihe von *Zellen geteilt* hat Auch innerhalb der übrigen Tonsillenanteile *der Lymphozytenkappe* ... *dem interfolli*kul... verzeichnen ... H³ Index etwa ... nach weiteren 24 Stunden also nach insgesamt 48 Stunden ist nahezu eine *nochmalige* Verdoppelung eingetreten Es sind jetzt nämlich 94 % aller Zellen *markiert* ohne dass inzwischen neues H³ Thymidin injiziert worden wäre

Wie verhalten sich nun die anderen beiden Anteile der Tonsille? Im interfollikulären Gewebe ist *nach* 48 Stunden lediglich eine Verdoppelung der Zahl markierter Zellen *erfolgt* Innerhalb der Lymphozytenkappe hat sich jedoch der H³ Index im Laufe von 48 Stunden verzehnfacht

Zur ... ion dieser Kurven soll vorerst bewußt vereinfacht werden

Es soll z. B. von der Annahme ausgegangen werden, daß die Zellen eines Gewebeteiles wenigstens hinsichtlich ihrer Generationsdauer gleich sind. Die in Wirklichkeit komplizierteren Verhältnisse können im Rahmen dieser Darstellung nicht diskutiert werden.

Der Zuwachs an markierten Zellen innerhalb des hellen Zentrums innerhalb von 48 Stunden paßt zu dem hohen H^3-Index nach 30 Minuten. Denn eine große Zahl teilungsbereiter Zellen läßt auf sehr lebhafte Teilungstätigkeit und andererseits auf eine kurze Generationsdauer der Zellen des betreffenden Gewebes schließen. Das bedeutet, daß die Zellen im hellen Zentrum alle dort entstanden sind oder entstanden sein können und daß die hellen Zentren wirklich Keimzentren sind. Der — relativ betrachtet — viel größere Zuwachs an markierten Zellen in der Lymphozytenkappe läßt demgegenüber den Schluß zu, daß die nach 48 Stunden dort vorhandenen markierten Zellen nicht aus Teilungen der wenigen, dort primär markierten Zellen hervorgegangen sein können. Sie müssen vielmehr an anderer Stelle entstanden und dann dorthin gewandert sein. Ähnliche Überlegungen gelten für die Zellen des interfollikulären Gewebes.

Es soll nun erörtert werden, ob sich weitere Anhaltspunkte finden lassen, die zu einer Erklärung der beobachteten Phänomene herangezogen werden können. Dazu muß untersucht werden, ob sich aus dem Verhalten der Markierungsintensität als Funktion der Zeit weitere Informationen ergeben, die den beobachteten Verlauf des H^3-Index stützen können. Bekanntlich erfolgt bei der Zellteilung zusammen mit der Teilung der Chromosomen eine gleichmäßige Verteilung des eingebauten Tritiums auf die Tochterzellen (Taylor, Koburg, 1960). Eine Tochterzelle in erster Generation hat daher etwa die halbe Silberkornzahl der Elternzellen.

Betrachtet man die Markierungsintensität über den Zellen des Kernzentrums nach einer Stunde und nach 48 Stunden, so erkennt man auf den ersten Blick, daß sich nach 48 Stunden die Silberkornzahlen über den Zellen der hellen Zentren, verglichen mit denen bei einer Versuchsdauer von einer Stunde wenigstens auf die Hälfte, meist aber auf den vierten Teil reduziert haben. Dies bestätigt, daß innerhalb der zur Beobachtung stehenden 48 Stunden tatsächlich ein bis zwei Zellteilungen erfolgt sein müssen. Innerhalb der Lymphozytenkappe sind die Verhältnisse anders. Betrachtet man die Lymphozytenkappe nach 48 Stunden, so findet man dort genau wie nach 30, 60 oder 120 Minuten einige wenige Zellen mit großer Silberkornzahl. Zusätzlich zu diesen wenigen stark markierten Zellen findet man nach 48 Stunden eine relativ große Zahl schwach markierter Zellen. Die Silberkornzahlen der schwach markierten Zellen liegen etwa in der Größenordnung von derjenigen der markierten Zellen des hellen Zentrums. Dies ist ein weiterer Hinweis darauf, daß die überwiegende Mehrzahl der dort nach 48 Stunden anzutreffenden markierten Zellen eingewandert ist.

Es konnte also nachgewiesen werden, daß die hellen Zentren schon unter normalen Bedingungen Orte außerordentlich reger Zellteilungstätigkeit sind. Ferner konnte wahrscheinlich gemacht werden, daß sowohl die Lymphozy-

tenkappe als auch das interfollikuläre Gewebe Zustrom an Zellen aus an deren Bereichen erhalten Es kann praktisch als sicher gelten daß diese Zellen aus den hellen Zentren stammen

Innerhalb der Lymphozytenkappe tauchen erste markierte kleine Lympho zyten schon nach 6 Stunden auf Im Bereich des Epithels sind nach einer Stunde die eindeutig als Lymphozyten zu identifizierenden Zellen nicht markiert Nach 24 Stunden finden sich bereits zahlreiche markierte kleine Lymphozyten sowohl in den Maschen des Epithels als auch im Krypten lumen und nach 48 Stunden sind schließlich alle in der Kryptenlichtung anzutreffenden kleinen Lymphozyten markiert Das bedeutet daß die Ent stehung von kleinen Lymphozyten aus größeren teilungsfähigen Vorformen bereits in weniger als 6 Stunden erfolgen kann und daß diese schon unter normalen Bedingungen nach 24 bis 48 Stunden in der Kryptenlichtung auf tauchen

RÉSUMÉ

A l aide de la thymidine H^3 qui est incorporée dans les noyaux lors da la synthese des acides desoxyribonucléiques, on peut suivre avec une technique autoradio-graphique la proliferation et la migration cellulaires dans les différentes structures tissulaires lymphatiques et dans l épithélium des cryptes amygdaliens La forma tion des cellules en effet se fait en prefence dans les centres germinatifs, mais aussi entre les follicules

SUMMARY

Autoradiography with H^3 Thymidine which is incorporated by the cells into heir nuclear DNA yields information on cellular proliferation and migration in the different structures of tonsillar lymphatic tissue and within the epithelium of the crypts. As a matter of fact, cell renewal occurs in the germinal centres and to a minor degree in the interfollicular tissue

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Moorenstraße 5, Düsseldorf, Deutschland

DISCUSSION

J. Jeschek: Ich glaube, daß wir auf Grund der wunderschönen Untersuchungen von A. Meyer zum Gottesberge den alten Streit, ob die Sekundärknötchen Keimzentren oder Reaktionszentren sind, auf friedliche Weise beilegen können. Wir müssen demnach annehmen, daß der kryptenferne Anteil der Sekundärknötchen, der nach dieser neuen autoradiographischen Untersuchungstechnik eine starke Zellteilung zeigt, die Funktion eines Keimzentrums aufweist, während die kryptennahe Lymphozytenkappe wohl als Folge einer Abwehrreaktion aufzufassen ist. Wir haben somit im Sekundärknötchen die Funktionen eines Keim- und eines Reaktionszentrums vereint, was ja auch verständlich wäre, da zur Abwehrreaktion eine vermehrte Anzahl von Lymphozyten erforderlich ist.

Meyer zum Gottesberge (Schlußwort): Der Gedanke von Herrn Jeschek ist sehr einleuchtend. Man könnte den alten Streit beilegen und die Sekundärfollikel als reaktive Keimzentren bezeichnen.

ODOUR PERCEPTION AND ENVIRONMENT CONDITIONS

ETTORE BOCCA and MARIA N BATTISTON
Milan and Sassari, Italy

From the Institute of Technical Physics (Head Prof G Bozza), Politecnicum of Milan and the E N T Clinic (Head Prof E Bocca) University of Sassari

Variations in humidity and temperature cause variations in the intensity of perception of the odours of pure substances In our research we aimed at effectuating a measure of this phenomenon which could be expressed numerically and with this in view, we chose the olfactory threshold, i e the minimal concentration of the substance under examination capable to originate an olfactory sensation

We set up an apparatus adjusted to give a wide range of well defined concentrations of odour substance It was found that, under equal circumstances the threshold concentration depends on the temperature and humidity of the inspired air

In the experiences referred to in this report variations in threshold values have been examined for most common humidity and temperature conditions A relationship has been determined which allows prevision of threshold values of pure substances in function of temperature The use of an olfactometer which allows exact concentration of odour substance in the air flux, has made direct and systematic measures of the threshold sensitivity possible The threshold value has been defined as the minimum quantity of odour substance per unit volume of air inspired (moles per litre) necessary to give the sensation

The results of preliminary tests show that the threshold value of each pure substance depends on

1 the type of substance
2 individual factors
3 environmental factors

Amongst the latter factors the threshold depends mainly on the temperature, the humidity the velocity of the air flow the atmospheric pressure, the presence of other odours and possibly the presence of contemporary stimulation of sensory terminations other than olfactory

Setting aside the study of individual factors and the relationship between the chemical nature of a substance and its threshold values we aimed at investigating the two environmental factors which are commonly used in characterizing the atmospheric conditions i e *temperature and humidity*

With this aim in mind we kept all the other above mentioned factors constant during all our tests and used the same subjects for all tests making

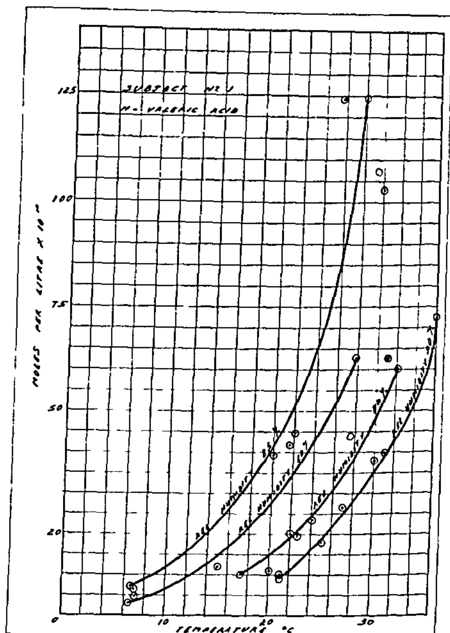


FIG 1

sure that they were in normal conditions—at least as far as their olfactory organ was concerned

Our main interest in this experiment was to confirm the hypothesis, previously formulated by us, that the olfactory sensation is due exclusively to that fraction of odorous substance which has been dissolved in the nasal mucus, and not to the substance present in the air, and, furthermore, that the threshold concentration in the mucus is practically constant for each substance and each subject

This hypothesis has already been supported by our previous research on latency and persistency of odorous stimuli

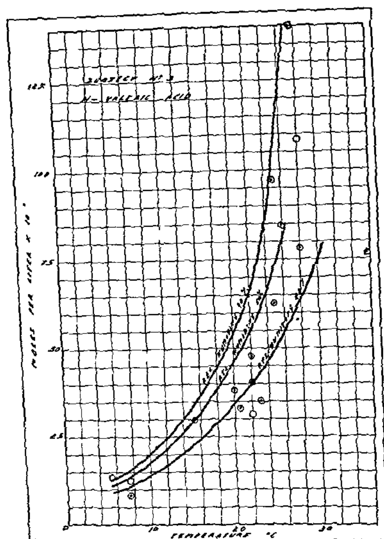


Fig 3

On the grounds of such hypothesis the following previsions may be formulated

1 We know that solubility of a gas in a liquid diminishes with the increase of temperature As a consequence and admitting that the concentration of an odorous substance in the mucus must be constant in order to excite an olfactory sensation at threshold values it may be assumed that the olfactory threshold should be higher at higher temperatures

2 Furthermore it may be supposed that the threshold concentration may vary also as a function of the relative humidity of the air in relation to vapour liquid equilibria of water in the air and in the mucus As a consequence the should rise when the relative humidity rises

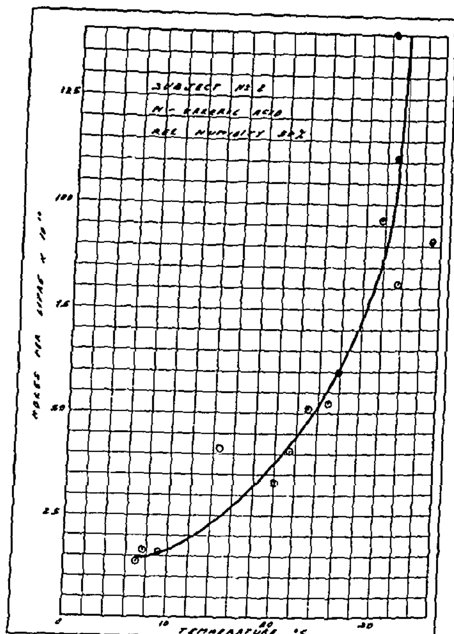


Fig 3

Technique of the Experiment

On the grounds of these premises, two sets of experiments were performed

1 The first series of tests was performed in order to establish whether the threshold varies with humidity and, if so, whether these presumed variations are in correlation with the relative humidity (defined as the ratio between the actual vapour pressure in the air and the saturation vapour pressure at the same temperature), or with the absolute humidity (weight of water vapour per unit volume of air) The influence of relative humidity upon thresholds was demonstrated experimentally

2 In a second series of tests the effect of temperature alone upon thresholds was then studied, keeping relative humidity constant

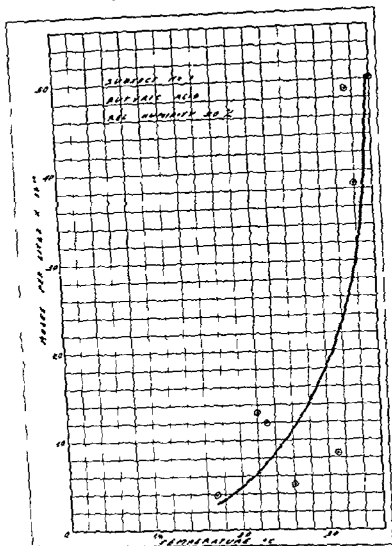


Fig 4

For the experiment the olfactometer previousl\ described in was used and the blast technique \was adopted Three subjects and three substances (butyric acid \aleric acid and citral) were used

The environmental conditions were convenientl\ determined and kept constant throughout the experiment The threshold was determined b\ a flux of odorized air, having a constant flow rate of ten cubic metres per hour— this being equal in our apparatus to a \elocit\ of 0 03 metres per second

The concentration of odorous substance in the air was originall\ set at far higher ratios than threshold and was then graduall\ reduced according to a pre established scheme

Ten sensibilit\ tests were made for each concentration and the positive

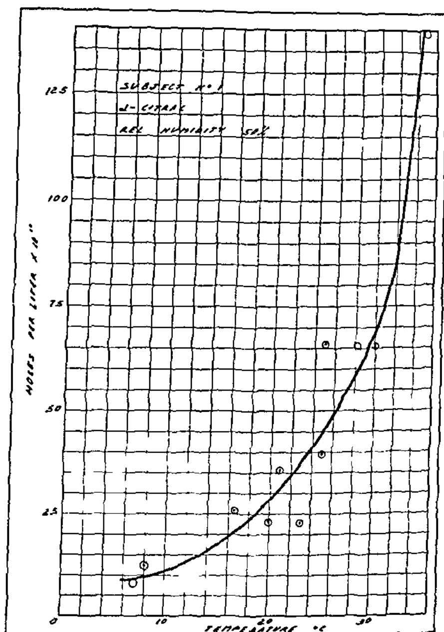


Fig 5

or negative results were noted The most probable threshold point was then calculated graphically by means of a Gauss curve based on the experimental results It was not possible to trace rational curves of the threshold concentration as a function of the absolute humidity, at constant temperature

The following graphs illustrate the experimentals results

Graph No 1, subject No 1, substance valeric acid
Graph No 2, subject No 3 substance valeric acid
Abscissae temperature in degrees centigrade
Ordinates concentration of threshold in moles per litre

The numbers next to the points on the graphs refer to the relative humidities As may be observed, it is possible to trace bands of relative humidity values along which the thresholds vary in function of the temperature

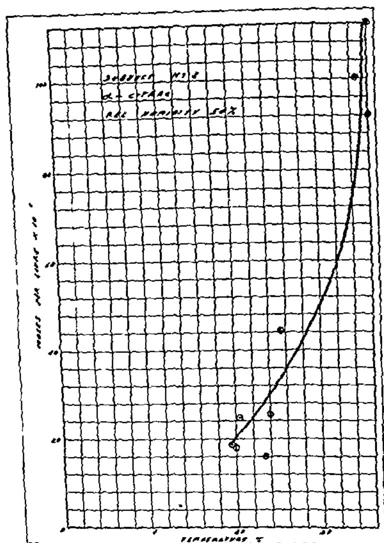


Fig 6

The curves which refer to constant relative humidity are all of the same exponential type and move towards the left when the relative humidity rises

It may also be observed that temperature influences the threshold values far more than humidity does

Graph No	subject No	substance
3	2	valeric acid
4	1	butyric acid
5	1	citral
6	2	citral
7	3	butyric acid
8	3	*citral*

Abscissae temperature in degrees centigrade
Ordinates concentration of thresholds in moles per litres

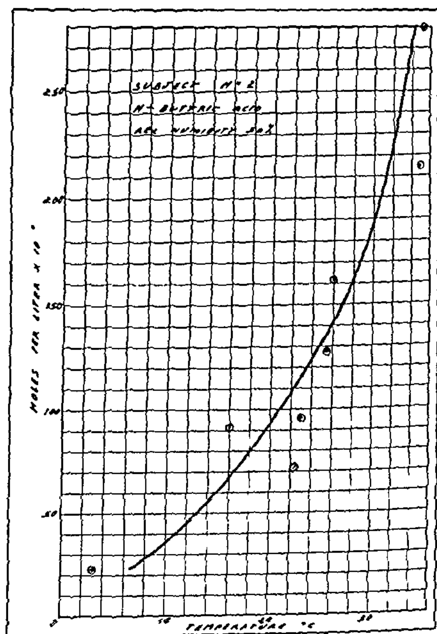


FIG. 7

The curves refer to a relative humidity of 50 % with different substances and different subjects. By this procedure the effect of humidity has been eliminated.

As may be observed, in all cases the thresholds follow an exponential curve in correlation with temperature and the slope of this curve varies according to the type of substance under consideration.

In the attempt of establishing a correlation between the variations of the threshold and those of the physicochemical properties of the odorous substances examined, Dr Battiston found that the former are in a definite relationship with the variations of the vapour pressure. More precisely the threshold concentration for a given substance in a given environmental

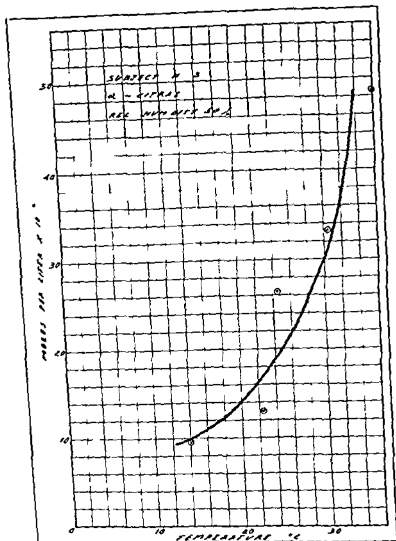


Fig 8

condition is within close approximation directly proportional to the vapour pressure when the relative humidity is kept constant

In other words for given values of relative humidity the ratio threshold *concentration vapour pressure is a constant for each subject and each substance*

Having determined this constant experimentally it is easy keeping all other environmental conditions constant to calculate the threshold concentration for other temperatures This is of great importance because it allows threshold values obtained in different circumstances to be reduced to a given temperature condition

Obviously there may have been interferences due to other environmental

conditions, although they were kept, as far as possible, constant throughout the experiment.

CONCLUSIONS

The olfactory threshold for a given substance and a given subject varies in correlation with changes in environment.

Experiments were made in order to determine the influence of variations in relative humidity and in temperature on olfactory threshold The following results were found.

1. Threshold concentration depends on the temperature and on the relative humidity of the air.
2. At constant relative humidity, the threshold rises with the temperature, according to an exponential law. Also, at constant relative humidity, the ratio between the values of the olfactory threshold and of the vapour pressure of the odorous substance under examination is a constant This constant rises with the rise of relative humidity
3. At constant temperature, the threshold rises when relative humidity rises. The temperature threshold curves for different humidity values show the same slope

RÉSUMÉ

On a déterminé les valeurs du seuil olfactif de sujets normaux pour l'eugenol, le citral, l'acide butyrique et valérianique en différentes conditions de température et d'humidité Les déterminations ont été effectuées à l'aide de l'olfactomètre tout récemment réalisé à la Polytechnique de Milan (Battiston) Les variations de la température (de +3° à +32°C) et de l'humidité (de 9 % à 90 %) causent des modifications significatives du seuil olfactif

Prof E Bocca, Viale Regina Giovanna 15,
Milano, Italy

DISCUSSION

F C Ormerod F C O asked Prof Bocca if he had investigated the threshold of olfactory sensation at temperatures at or about blood temperature

The sensitivity increases from zero to saturation humidity and up to 32°C It is known that the sensation of taste has an optimum of 30°C

Is there such an optimum for smell and if the temperature were raised much above 32 does Prof Bocca think there might be a fall in sensitivity? It is an experience in very hot countries that the sensation of scents and other smells is less in the heat of the middle of the day than in the cool of the morning and evening

E Bocca (Reply) I agree with Ormerod that experiments with changes of temperature should be extended beyond our limit of 32°C The fact is that, conditioning as we are the temperature of the whole room and not only of the flux of air, as high temperatures as 37° or more could be poorly tolerated by the subject, thus introducing more causes of error in our determinations

VARIATIONS IN NYSTAGMOID RESPONSE TO STIMULATION CAUSED BY A NUMBER OF PHYSICAL, MENTAL AND CHEMICAL FACTORS

F C ORMEROD
London Great Britain

The influence is described on the movements of the eyes as recorded by electro nystagmography of variations in the environment of light and sound in mental alertness occupation and relaxation in the open or closed state of the eyes in the activity or passive state of the gaze and of the ingestion of a variety of chemical substances

Eyes Open or Closed

In testing for nystagmoid movements of the eyes which result from stimulation of the vestibular labyrinth it is not infrequently the case that nystagmus cannot be observed visually—with the eyes open and in most cases with a certain and unavoidable amount of fixation of gaze In such cases with the eyes closed and by electro nystagmography it is frequently possible to record nystagmoid movements which may be of considerable amplitude Electro nystagmography does not reveal non existent movement of the eye balls and it is usually possible to recognise visually the existence of nystagmus if it is detectable by electric means By the ability however to magnify on the written record the range of the eye movements and to vary the speed of their recording it is possible to analyse and measure what by visual me[illegible]

[illegible]

[illegible] nystagmus of square waves and of variations in the speed of the slow component of nystagmoid movement It is however the closure of the eyes and the absence of the inhibiting effect of light and of other disturbing influences which give free play to the nystagmus and give this method of accurate recording of movement of the closed eyes even during rotation and caloric stimulation its value

It is not only in the recording of nystagmus due to artificial stimuli but also in the recording of spontaneous nystagmus that this method is of such value A patient recently seen who suffered from advanced Meniere's disease did not appear to have any spontaneous nystagmus on visual inspection and showed no certain response to caloric testing with the eyes open On repeating the tests with the eyes closed and by electric recording vigorous and regular nystagmus was observed It was noted however that by both warm and cool tests of the right ear and by the warm test of the left ear the

quick component was to the left and the duration of the nystagmus was indefinitely prolonged. The cool test of the left ear alone produced a nystagmus to the right. After a suitable interval, electric recording of the ocular potentials showed that there was a spontaneous nystagmus to the left and that the results apparently obtained by douching the right ear by warm and by cool water were merely this spontaneous nystagmus, which was caused by the total inactivity of the right vestibular labyrinth. The nystagmus obtained by warm syringing of the left ear did not vary the spontaneous nystagmus in progress, but the cool test did reverse this nystagmus for the usual period of some three minutes, followed by a resumption of the underlying spontaneous movements. These phenomena were easily recorded by electro-nystagmography, but were undetectable with the eyes open. Testing by this electrical method with the eyes open is so uncertain, owing to the differing response by different subjects, that its value is negligible.

It is easier to recognise the end point of nystagmus by electrical recording than by the visual method as it becomes slower and of less amplitude, as the end point as recorded is clear-cut and definite, and it is also easier to recognise where primary nystagmus ends and where after-nystagmus or secondary nystagmus begins. The reversal of direction, or the occurrence of square waves is difficult to identify by the visual method but easy by electro-nystagmography. The records made by this method are permanent and precise and they enable the speed of the slow component to be measured with accuracy.

It was found that opening the eyes during electrical recording immediately stopped the nystagmus, which was replaced by a prolonged slow deviation of the eyes in the direction of the previous slow component and this was followed by an equally slow and prolonged movement in the opposite direction. On closing the eyes again, nystagmus of the same direction and rhythm as before was resumed—if the period during which the eyes were open was short and the effects of the original stimulus had not worn off. It is important that the testing room should be in relative darkness and not brightly illuminated so as to avoid the glow through the eyelids, or flickering light through not too firmly closed lids.

Environment of Sound

It is also of importance that there should be an absence of vicarious noise in the testing room as it is the experience that such sounds interrupt the rhythm of nystagmus. Conversation among third persons in the testing room tends to inhibit nystagmus and any sudden movement or noise may have the same effect. It was observed by R. Ormerod that in complete silence some individuals gave a poor or no nystagmoid response, but when subjected to simple conversational matter, a better and more regular response was obtained. The playing of music did not have this effect and in some subjects it led even to a reduction in the amplitude or in the duration of nystagmus. It is probable that the act of listening to conversation reduces a possible degree

of central inhibition and that music does not at any rate in some individuals have this effect McLay has made use of these phenomena and delivers controlled voice by means of a tape recorder and amplifier and thus subjects the individuals being tested to standard conversational stimulus and makes the conditions under which the tests are being carried out uniform

Individual Variations in Reaction

It has been found however that even by electro nystagmography there is a divergence among normal subjects in their response to similar stimuli and that even in a dark and quiet environment some may give very slight response to ordinary experimental stimuli It is rare to find individuals who give exaggerated reaction to such stimuli but some adapt very quickly and cease to respond while others are able to control nystagmus at will It has not been established that fear or other emotions create inhibition—probably the reverse is the case One patient who came from another country and spoke no English who was very much disturbed by the vertigo from which she suffered and very frightened by the examination and by the various electrical and other apparatus was so upset by the subjective sensation of vertigo on the ear being douched that she screamed out loudly shook her head from side to side and was with difficulty restrained The electrode pick ups fortunately remained in position and a perfect record of normal nystag mus was obtained in spite of all the disturbance the fear and the emotion having apparently eliminated any inhibiting influence

Effect of Mental and Visual Processes

Sokolovski of Skopje working at the Institute investigated the effects on nystagmus of a number of mental and visual processes During and after rotation he asked the subjects of his tests a number of questions the answer to which required a certain amount of mental arithmetic and in other tests the subjects wrote down extracts from the daily newspaper which were dictated to them These tests were carried out in a quiet and dark room It was found that the mental processes involved in these exercises were suf ficient to lift a certain amount of inhibition and there was an increase in the number of nystagmoid beats in their frequency and in the duration of the nystagmus There was also a relatively greater increase in the amplitude of the angular movement of the eyes and in the speed of the slow component

Further tests were carried out which involved some degree of fixation of the gaze In one test as soon as rotation ceased the subject proceeded to count drops of water which fell from the nozzle of a douche can and which were just illuminated in an otherwise darkened room In the other test a very small spot of dim light was carried round with the rotating subject again in an otherwise darkened room The subject looked throughout at this light during and after rotation In both of these tests there [illegible] degree of [illegible]

and the duration of the beats. The result of this series of experiments shows the degree to which simple mental processes lift inhibition from the nystagmoid responses to stimulation and also that ocular attention and especially fixation lead to considerable inhibitory effects. It is also interesting to note that in these investigations of the decreasing and increasing inhibition the greatest is shown in the amplitude of the nystagmoid stroke and in the speed of its slow component.

Effect of Ingestion of certain Chemical Substances

Bochenek of Warsaw, also working at the Institute, investigated the effects on the nystagmoid responses to caloric and rotatory stimuli and found that, on the whole, when the tests followed the ingestion of barbituric acid derivatives, antihistamines and parasympatholytes, the degree of inhibition of the various factors was about the same for each individual drug.

After alcohol, however, the inhibition is relatively more marked in the amplitude of the nystagmus than in the duration and number of beats. The inhibitory effect of alcohol is also more marked after rotatory than after caloric stimulation.

Of the various substances used in these tests, the barbiturates produced the greatest amount of inhibition of ocular movement and therefore the greatest degree of static control, but at the same time they gave rise to a greater number of unpleasant subjective sensations. The antihistamines gave almost as great a degree of inhibition but the subjective sensations were considerably less. The parasympatholytes gave a relatively poor amount of inhibition. As a remedy for the various forms of travel sickness it appears therefore that the antihistamines give the best results.

The phenomena which have been described illustrate how the many factors which may be present can influence the results of testing the static labyrinth and give perhaps misleading information. Most of these factors can be eliminated and by so doing or at least by recognising them, possible mistakes in interpretation may be avoided.

RÉSUMÉ

On décrit l'influence sur les mouvements des yeux, enregistrés par l'électro-nystagmographie, des variations en l'environ de la lumière et du son, dans la vigilance, l'occupation ou le relâchement mental, dans l'état ouvert ou fermé des yeux, dans l'activité ou l'état passive du regard et de l'avalement d'une variété des substances chimiques.

ZUSAMMENFASSUNG

Es wird der Einfluss auf die Augenbewegungen beschrieben, registriert durch Elektronystagmographie, auf Verschiedenheiten der Umgebung von Licht und Klang, bei geistiger Wachsamkeit, bei Beschäftigung und im Ruhezustand, bei geschlossenen und offenen Augen, auf aktiven und passiven Zustand des Blickes und nach Einnahme verschiedener chemischer Substanzen.

37 Portland Place, London, W. 1, England.

THE ACTION OF BRONCHIAL MUSCLES

V Negus
London Great Britain

The oto laryngologist has the welfare of the nose and upper respiratory passages in his keeping with the responsibility of ensuring a free passage of air it seems fitting that he should take some interest in the disposal of this air on its way to the pulmonary alveoli In my time the laryngologist played an important role in the diagnosis and treatment of lung diseases by broncho scopic methods and his training in the use of monocular vision gave him great advantages in this respect

Bronchoscopy can throw much light on the anatomy and physiology of the respiratory passages and examination of the bronchi of children and asthmatics in particular affords a great deal of information as to the action of bronchial muscle Comparative anatomy and histology is also of con siderable value in this respect It is necessary to have some detailed know ledge of the anatomy of the tracheo bronchial tree a subject of some dif ficulty the investigations of Dr Lynne Reid and Dr Engel are of particular help in this direction

The larger bronchi of man have much cartilage in their walls partly in the form of rings the smaller bronchi also have cartilage but in less amount and in places as isolated plaques Both subdivisions are alike in having the lumen made more or less rigid by this cartilaginous support The lower part of the air passages has no cartilage and this includes the terminal bronchioles and the respiratory bronchioles

It is a general rule as seen in the nose and paranasal sinuses that non collapsible cavities have a ciliary system to remove debris and excess fluid from the lumen while collapsible cavities such as the gastrointestinal tract and the bronchioles rely on muscular contraction to expel contents Cilia are found therefore only in the rigid walled cavities and histological ex amination shows their absence in the stomach and intestines in the pharynx and also in the bronchioles where they are non existent or very scanty A few isolated cilia are of no use they must form a continuous sheet if they are to propel secretion or debris

The support of the walls of bronchi by cartilage is accompanied by a supply of mucous glands and goblet cells cartilage and glands gradually diminish from above until in the finer tubes both are absent The muscular supply on the other hand increases as the air passages are traced down until in the bronchioles it is well developed

In a previous communication to the Collegium in 1962 I made suggestions as to the function of mucus and supported the views advanced by evidences of comparative biology the conclusion was that mucus has a water proofing

function both on the surface of animals such as earthworms slugs and eels and also on mucosal surfaces Its presence prevents excessive passage of water inwards by osmosis and outwards by transudation by virtue of its very *long molecules* which form a meshwork and act like a sponge in restricting the escape or the absorption of water

If it is true that a covering of mucus has a water proofing action on the surface of the body of certain invertebrates amphibia and fish and also in the respiratory and alimentary passages it is necessary to examine the relationship of mucus to ciliary streams Usually it is supposed that mucus is present to facilitate the action of cilia but this explanation does not hold in the food passages

A suggestion made by Dr Forbes Professor of Anatomy in the Medical School of Yale University is in my opinion of great value it is to the effect that instead of mucus being present for the benefit of cilia it is the other way round that cilia are provided to remove the excess of mucus and transudate

This immediately throws light on the problem and allows water proofing to be regarded as the primary function of mucus with provision of ciliary streams in those cavities incapable of closure by muscular contraction

For instance in the posterior nasal passage or naso pharynx the upper part is non collapsible and is provided with cilia while the lower part with its encircling superior constrictor muscle relies for its clearance of debris on muscular action

And similarly in the rigid walled bronchi there are cilia while in the collapsible bronchioles muscular action serves to clear the lumen

Another function of bronchial and bronchiolar muscle is connected with dead space air It is important to expel this air which takes no part in the diffusion of oxygen and carbon dioxide contraction of bronchial and bronchiolar muscle during expiration will help in this respect There is in the trachea of the horse a broad sheet of muscle attached on the inner surface and serving to pull on the overlapping tracheal rings and thus to diminish the lumen which must be of considerable assistance in this quadruped with its long tracheo bronchial tree and enormous dead space

Anyone who has practiced bronchoscopy will have noticed the very considerable expiratory diminution of the lumen of bronchi and their branches and even of the trachea especially in children and in asthmatics

Furthermore in removing a foreign body such as a bead impacted in a secondary or tertiary bronchus it is necessary after grasping the object with forceps to pull it upward only during inspiration during expiration it is held firmly by muscular contraction

The muscular system being arranged as a meshwork not only diminishes the lumen of a bronchus but also reduces its length

There is another aspect of the action of bronchiolar muscle and that is assistance in the mixing of air in the alveoli the usual explanation of this mixing relates it to diffusion but that is a relatively slow process since the alveoli change but little in size during the phases of respiration In the

smaller branches, the muscle surrounding the bronchioles, contracting at the commencement of expiration, will not only propel some air outwards, but will also displace a certain volume in the opposite direction, that is into the saccules and alveoli, in this it will help in air mixing in what may be called the 'blowback' mechanism

It is desirable to examine in rather more detail the water proofing of the bronchioles they have no supply of mucus except in certain pathological conditions in which some excess secretion fills their lumen and even reaches the alveoli It might be thought, therefore, that in these finer tubes there would be uncontrolled passage of water in and out of the mucosa, causing oedema or shrinkage, but the finer respiratory tubes are related to pulmonary capillaries in which the hydrostatic pressure is low and is counterbalanced by the osmotic pressure of plasma protein Consequently, transudation is unlikely, while oedema need not occur because the pulmonary capillaries are capable of taking up condensed moisture, supposing it to be deposited by inspired air

To summarise these proposals they are that muscular contraction can eliminate the lumen of bronchioles and can thereby remove secretions and also dead space air while at the same time helping in mixing unused air from the anatomical dead space with the partly used up gases in the alveoli

Hill Farm Lodge, Haslemere, Surrey, England

DISCUSSION

E Huizinga 1 Sir Victor has spoken of a primary function of the mucus as an important function of the sero mucus glands I perfectly agree There is much interest now in chronic bronchitis So many patients die from emphysema or cor pulmonale There is now much literature about the anomalies found at broncho graphy and in microscopy of anatomical specimens The most characteristic anomaly of chronic bronchitis (recently it was again demonstrated by the pathologist Lynne Reid) is a hypertrophy of the sero mucus glands It gives the impression that a disturbance of this function must be very important also in pathological cases

2 Sir Victor demonstrated a slide about an active function of the bronchial muscles during respiration It is difficult to accept an active function, because it must change often during respiration and the smooth muscles of the bronchi probably cannot do it There are of course often very important changes of the lumen of the bronchi during respiration But they are not due to an active function of the smooth muscles The changes are passive as was also demonstrated in this country by Ellis A permanent tonic action of these muscles is well known in asthma

H A E van Dishoeck 1 One of the important functions of the mucosa of the nose is the moistening of the inspired air If this function is counteracted by the sealing-off function of the mucous what is the solution of this contradiction?

2 The primary function of the mucus together with the ciliated epithelium is to constitute the moving layer of mucus (tapis roulant) by means of which inhaled bacteria, allergenes and small foreign bodies are removed to the pharynx to be swallowed

3 As long as it is not proven otherwise I think that the widening and narrowing of the bronchis is mainly passive Only occasionally a change in the tonus (e g as a protection against the penetration of mucus in the alveoli) is an active function

A C Hilding As usual Sir Negus brings us new and stimulating ideas

We have long been aware of the muscles in the tracheo bronchial tree and it has been suggested that they produce peristalsis as in the intestinal tract This seemed most unlikely in spaces and tubes that must remain patent for the transmission of gas air But Sir Negus has pointed out that the narrowing or closure of the terminal bronchials during expiration only could be possible Under these circumstances peristalsis is thinkable The reduction of dead space (150 cc in the human tracheo bronchial tree) not only appears logical, but he has actually observed it This action would account for the overlapping of the cartilages which he has shown in the horse I have observed a similar overlapping in one of the small animals upon which I have worked I believe it is the hen The cow has a strong band of muscular across the posterior third similar to that which he has shown in the horse The arrangement of cartilages is very different but the muscle band undoubtedly serves the same purpose of reducing dead space

J Jeschek Zu den wirklich interessanten und aufschlussreichen Ausführungen von Sir Victor Negus über die respiratorische Funktion der Trachea und des Bronchialbaumes möchte ich noch ergänzend bemerken dass wir auch im Larynx während der Respiration Bewegungen der Stimmbänder sehen können die ähnlich denen der Bronchien verlaufen Semon hat erstmals diese beschrieben und angenommen dass in einem gewissen Prozentsatz solche Bewegungen der Stimmbänder konstitutionell bedingt auftreten Vor einigen Jahren habe ich eine grosse Anzahl von Patienten mit respiratorischen Bewegungen untersucht und konnte feststellen dass bei einer respiratorischen Insuffizienz wie z B bei Asthma Emphysem Silikose und ähnlichen Lungenerkrankungen gehäuft Bewegungen der Stimmbänder der Epiglottis und des weichen Gaumens während der Atmung zu beobachten sind Auch bei gewissen zerebralen Prozessen wie z B bei der Pseudobulbärparalyse kommt es wahrscheinlich durch Verminderung der zentralen Rindeninhibitionen oder durch Reizung des Atemzentrums oder übergeordneter Integrationsgebiete im Diencephalon zu vermehrten respiratorischen Bewegungen Interessant ist es nun dass analog dem Kontraktionsvorgang der Bronchialschleimhaut während der Exspiration bei obig erwähnten Fällen eine Verengerung der Glottis erfolgt während die Epiglottis und der weiche Gaumen gehoben werden Je höher die respiratorische Insuffizienz um so stärker ist das Ausmass dieser Bewegungen und um so weiter nach Median werden die Stimmbänder verschoben Wenn wir bei den lehrreichen Untersuchungen von Sir Victor Negus über die physiologischen Vorgänge der Trachea und Bronchien bei der Atmung den Larynx miteinbeziehen und so den Respirationstrakt als funktionelle Einheit betrachten werden wir vielleicht noch weitere Einsicht in die komplexen respiratorischen Vorgänge erhalten können

Sir Victor Negus (Reply) to Huizinga The function of mucus as a water proofing agent has a direct relation to bronchitis and asthma In these diseases there appears to be increased permeability of the bronchial mucosa and to resist entrance of water by osmosis the goblet cells and in places submucous glands pour out an increased amount of mucus This misguided effort leads to filling of bronchioles with secretion with consequent embarrassment of respiration Not only is the mucus anchored to the goblet cells as described by Hilding but in addition there is a diminution or absence of cilia since most cells are transformed to mucus producing

goblet cells As regards bronchial and bronchiolar muscle I am assured by neuro physiologists that plain muscle can easily contract at the rate of respiration con traction occurs during expiration and is active and clonic

To van Dishoeck The reply is that mucus has more than one function but the primary function appears to be the control of passage of liquid inward by osmosis or outward by transudation Entrance of secretion into the acini or alveoli could not be prevented by contraction of bronchial or bronchiolar muscle because this occurs during expiration if it took place during inspiration it would prevent entrance of air which would be disastrous

To Hilding He has spoken of peristalsis and that seems to be probable in the re moval of dead space air to prove that it occurs is difficult but it is hoped that in vestigation by electronic methods may give information

It is interesting to hear of the overlapping cartilages of the fowl and of tracheal muscle in the cow

To Jeschek He speaks of glottic movements but there is no problem here, since they are of assistance to the mechanical air mixing mechanism mentioned



LARYNGOSCOPY PERFORMED UNDER GENERAL ANAESTHESIA THROUGH A COMMISSURE LARYNGOSCOPE

B Blondal M Balslev Jorgensen and H K Kristensen
Copenhagen Denmark

From the Department of Otolaryngology and the Department of Anaesthesia, Rigshospitalet (University Hospital), Copenhagen

The problems of direct laryngoscopy performed under general anaesthesia are presented Thereupon the authors describe a method for direct laryngoscopy under general anaesthesia in which the patient is ventilated direct through Jackson s anterior commissure laryngoscope A total of 237 anaesthesias have been performed without major complications attributable to the method The technique is recommended, as it is simple and applicable for patients of all ages

A team performing diagnostic and therapeutic procedures on the larynx under general anaesthesia will meet various difficulties due mainly to the fact that the surgeon as well as the anaesthetist must have access to the patient s airways simultaneously or alternately

To the surgeon the most important thing is to have free access to the larynx at any rate during periods so long as to permit sufficient inspection and short lasting surgical procedures At the same time the anaesthetist has to secure alveolar ventilation sufficient to prevent major shifts in arterial oxygen saturation and carbon dioxide tension

Among other but easily solved problems it may be mentioned that as an electric apparatus is used explosive anaesthetics are out of the question An ideal anaesthesia or analgesia for direct laryngoscopy moreover requires that the patient should be awake and have normal reflexes as well as muscle tonus a few minutes after the procedure Lastly the anaesthetist of course wants a good illumination in order to detect the slightest changes in the patient s colour

General anaesthesia for laryngoscopy may be administered in various ways

The inhalation method in which the patient breathes spontaneously requires a non explosive anaesthetic and deep anaesthesia Keeping up respiratory activity as well as a suitable muscular relaxation to give free access to laryngoscopy is difficult and time consuming Moreover the risk of aspiration to the respiratory tract is increased during the postoperative period owing to inhibited laryngeal reflexes

The same applies to laryngoscopy under general analgesia which may be obtained by intravenous administration of pethidine (Demerol®) which is



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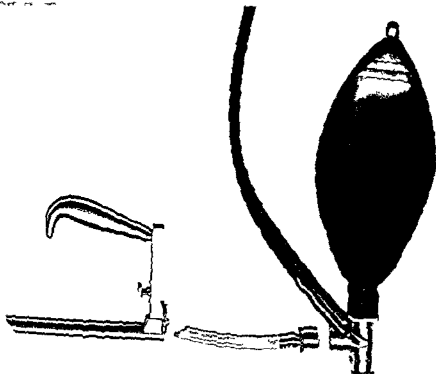


Fig 1

Premedication is administered 1 1½ hours before taking the patient to the operating theatre using atropine 0 1–0 5 mg and morphine 1 10 mg or an equipotent dose of pethidine (Demerol®)

Before anaesthesia is induced the patient breathes pure oxygen for 3 5 minutes This procedure has proved capable of maintaining an almost normal arterial oxygen saturation for up to 10 minutes during an apnoeic period (Lachman Long & Krumperman 1955) Thereupon the anaesthesia is induced by intravenous injection of a short acting barbiturate (Narcodorm® = enit omal natrium N F N) The anaesthesia is maintained by intermittent doses of the barbiturate while complete muscular relaxation and thereby apnoea are obtained by intravenous administration of suxamethonium chl ride

When the patient is relaxed the laryngoscope can be introduced and endolaryngeal inspection or intervention may be carried out for a so to speak unlimited time At 1½ 3 minute intervals the laryngoscope is used as an anaesthetic tube being carried right to the glottic chink The above mentioned plastic tube with respiration valve + balloon is mounted and the patient is ventilated with pure oxygen or a mixture of nitrous oxide oxygen

As soon as the plastic tube has been removed the surgeon can continue As there is no need to remove and re insert the laryngoscope for each period

said to have a special depressor effect upon laryngeal and pharyngeal reflexes (Ruben & Andreassen 1951 Knudsen Rasmussen Ruben & Traun Pedersen 1958)

Direct laryngoscopy may be performed on patients rendered apnoeic by muscle relaxants while the anaesthesia is induced and maintained by intermittent intravenous injections of a short acting barbiturate (De Graaf Woodman 1961) The advantages of this technique are that all muscular activity is completely abolished and that the patients quickly regain muscle tonus cough reflexes and consciousness

On the other hand this method does not always allow the surgeon sufficient time In order to compensate for the hypercarbia and hypoxia caused by a fairly long lasting state of apnoea several methods have been devised aiming at the maintenance of various degrees of respiratory function

(1) Insufflation of oxygen into the upper air passages through a thin catheter introduced through the mouth or the nose (Schweitzer & Howland 1959 Young 1958 Helperin & Waslow 1959) This however gives no elimination of carbon dioxide and moreover restricts the laryngoscopic field in cases where the tube is passed down through the aperture of the larynx

(2) Artificial ventilation by various types of cuirass respirators (Green & Coleman 1955 Helperin & Waslow 1959 Knudsen Rasmussen Ruben & Traun Pedersen 1958) *It may be a disadvantage that arranging the* respirator is a laborious process and requires much space Moreover the method does not necessarily secure adequate ventilation By a cuirass respirator a sufficient ventilation can be maintained only in patients of ordinary body build with a normal lung chest function (Juhl & Thorshauge 1957 Safar 1958)

(3) Controlled ventilation by an endotracheal tube (Priest & Wesolowski 1960) This method is inapplicable for children and even in adults the laryngoscopic field is appreciably restricted

Present Investigations

Before an anaesthetic department was established at the University Hospital the E N T Department did the laryngoscopies under general anaesthesia by the open drop ether method Despite premedication with atropine the procedures were generally greatly hampered by pronounced secretion

After some years use of a method by which the patients received oxygen through a thin tube in the trachea the laryngoscopies have been carried out since 1958 under general anaesthesia by a technique which appears simple and applicable for patients of all ages

The principle of this method is to connect airtight to the proximal end of the anterior commissure laryngoscope (Jackson) an obliquely cut short plastic tube through which the patient may be ventilated At its distal end the laryngoscope is so adapted to the laryngeal vestibule that when it is pressed down towards the anterior commissure the patient can be effectively ventilated without any notable retrograde waste of air

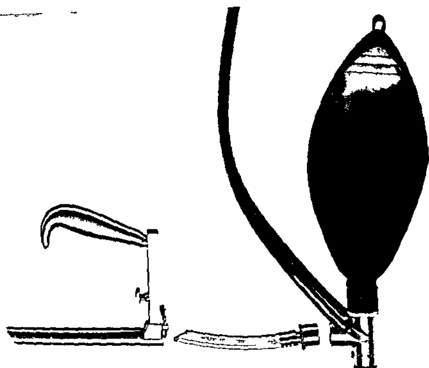


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As soon as the *plastic tube has been removed the surgeon can continue.* As there is no need to remove and re-insert the laryngoscope for each period

of ventilation traumatization to the tissue is avoided and the surgeon feels considerably more confident

During the past four years this method has been used on a total of 156 patients 117 males and 39 females ranging in age from 3 to 84 years. Seven patients were under 10 and 49 over 60 years of age. A total of 237 laryngoscopies were performed as many patients had several some (usually patients with laryngeal papillomas) even 10 or 11. In nine instances the laryngoscopy was combined with bronchoscopy and/or oesophagoscopy.

Twenty nine *patients had mild heart disease* i e *a history of coronary* occlusion or slight arterial hypertension. Seven had severe or moderately severe *hypertension. Among other complicating diseases it may be mentioned* that five had chronic bronchitis and asthma two had rheumatoid arthritis treated with cortisone and *four had diabetes mellitus*. One patient had a history of thoracoplasty removing the five uppermost ribs one had epilepsy and one had a history of a laryngeal operation (laryngofissure).

In the present series there were no complications necessitating an interruption of the anaesthesia before the laryngoscopy had been completed as planned. In four patients fractures of or chipping off of enamel from the incisors occurred and one patient got a contusion haematoma on the lower lip. The most serious complication occurred in a two year old child. After laryngoscopic removal of an eggshell—which had been impacted in the larynx for 4 days and had caused a large oedema—she developed severe stridor and required immediate tracheotomy. The further course was uneventful. The tracheal cannula could be removed on the *7th* day and the patient was feeling well when discharged on the 10th day.

Owing to the possibility of complications the *patients* are usually admitted on the day before laryngoscopy and discharged on the day after. In six cases *however the procedure was done on an out patient basis* and after having rested for a couple of hours the patients went home.

ZUSAMMENFASSUNG

Die Probleme unter allgemeiner Anästhesie durchgeführter direkter Laryngoskopie werden beschrieben. Darauf beschreiben die Verfasser eine Methode für direkte Laryngoskopie unter allgemeiner Anästhesie in welcher der Patient durch Jacksons Vorder Kommissur Laryngoskop ventiliert wird. Es sind insgesamt 237 Anästhesien ohne *grössere dieser Methode zuzuschreibenden Komplikationen* durchgeführt worden. Die Technik wird empfohlen da sie einfach und für alle Altersklassen geeignet ist.

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Department of Anaesthesia and Otolaryngology
Rigshospitalet Copenhagen Denmark

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PREOPERATIVE ASSESSMENT OF HEARING LOSS

O Hallén, G Lidén and B Nordlund,
Goteborg, Sweden

From the Department of Otolaryngology (Head Prof G Herberts) and the Laboratory of Audiology (Head Ass Prof G Lidén), Sahlgrenska Hospital, University of Goteborg

The aim of the preoperative investigations of patients with hearing loss, including clinical, X-ray and audiometric examination, is to answer the following questions

How great a handicap does the patient have from his hearing loss? Is there any active infection, irritation or cholesteatoma present, which can defeat an operation to improve hearing? How well are the Eustachian tubes functioning? Are there any morphological or functional defects in the ear drum or ossicles? How well are the oval and round windows functioning? How good is the sensori neural function? Not until these questions are answered is it possible to judge whether there are any indications for operation and what type of operation should be performed

Since the beginning of the 1950's the surgical treatment of conductive hearing loss has been developing steadily Operations for the improvement of hearing are today a reality and include practically all types of conductive loss Parallel with this development, audiological diagnostic procedures have also been refined and extended, so that one can now determine the site and type of lesions with reasonable accuracy before operation This is of course a great advantage for both patient and surgeon To the patient, it gives an increased sense of security that his case has been carefully and thoroughly tested, and the risk of unnecessary operation thus reduced To the surgeon it gives the possibility to plan his operation beforehand and thus to avoid improvising The purpose of this paper is to present a brief guide to the questions that arise before operation and to show how, by combining the results of various diagnostic tests one can obtain practical clinical answers

The following are the main questions to be considered during the preoperative investigation

1 How great a handicap is the patient s hearing loss?
2 Is there any active infection, irritation or cholesteatoma present which can prevent an operation from improving the hearing?
3 How well are the Eustachian tubes functioning?
4 Are there any morphological or functional defects in the eardrum or ossicles?
5 How well are the oval and round windows functioning?
6 How good is the sensori neural function?
7 Are indications for operation present?

Preoperative investigation consists of the following parts

1 Clinical examination comprising case history, physical examination tubal function test preliminary estimation of hearing
2 X ray examination
3 Audiometric examination consisting in part of routine tests and in part of various special tests
4 Discussion of the case the results of the clinical X ray and audiometric examinations are considered in relation to the operative possibilities

CLINICAL EXAMINATION

Case history

The examination of all cases of hearing loss begins with a careful case history Particularly when it is a question of chronic otitis it is important to determine the type of secretion and the length of the acute phases and dry periods Indirectly in taking a thorough case history one gets a hint as to the mentality of the patient and the possibility of co operation in the future

Physical examination

In addition to the examination of the ear itself it is important that the patient be given a general physical examination that is sufficiently thorough to expose conditions which may be hazardous for the operation planned The other parts of the E N T region especially should be examined carefully As far as the ear examination is concerned it should be the rule that all cases where the usual physical examination does not reveal a completely normal eardrum should be examined microscopically

Tubal function

Normal tubal function is normally a prerequisite for tympano plastic surgery On the other hand a reduced tubal function is often the cause of a chronic middle ear condition It is therefore from a diagnostic as well as from a therapeutic viewpoint of the greatest importance when examining the middle ear to get a correct estimate of tubal function With an intact eardrum the function of the tube can be tested according to Toynbee Valsalva or Politzer or by catheterisation It is advantageous to make the observations of the movements of the eardrum in these tests in connection with a microscopic examination In patients with a perforated eardrum tubal function is judged most easily with a stethoscope In difficult cases insufflation of air through the tube at varying pressure gives a more accurate impression of the condition of the tube

Preliminary assessment of the hearing

Just as it would be wrong to omit heart auscultation because X rays and ECG are available, so it would be wrong to neglect tuning fork, conver

sation, whispered voice and noise tests just because one has equipment for audiometry. For the examiner who uses them daily these tests quickly furnish valuable information about the hearing loss quantitative as well as qualitative. A positive Rinne *excludes as a rule a gap greater than 20 db between air and* bone conduction. A negative Rinne usually means a gap greater than 30 db. The conversation test often gives a rather good estimate of the patient's handicap and hearing loss.

The audiometric assessment is made easier if the examiner has from the beginning an approximate impression of the type and degree of hearing loss. Finally, it must be pointed out that only by carrying out clinical and audiometric hearing tests *parallel* with each other can one avoid many of the pitfalls which undeniably exist in otological diagnosis.

X-RAY EXAMINATION

The development in recent decades of X-ray diagnosis, and especially of tomography, has proved to be of great assistance in the preoperative evaluation of cases of hearing loss. X-ray examination may therefore be said to be *obligatory* in all cases, *with the possible exception of those with clinically* obvious otosclerosis.

AUDIOMETRIC EXAMINATION

The aim of the audiometric examination should be to obtain as complete answers as possible to three questions:

1. *How great a handicap does the patient have from his hearing loss?*

A correct answer to this question, supplemented by a knowledge of the patient's situation in life, enables one to judge how important it is for the patient to have his hearing improved.

2. *How great a portion of the hearing loss is caused by conductive impairment?*

The answer to this question gives the theoretical basis for surgical improvement of hearing.

3. *What is the cause of the conductive impairment?*

The more completely the audiometric examination can answer this question, the greater the possibility of estimating the chances of success of an *operation* and of planning the operation in detail.

Routine Tests

Tone and speech audiometry are carried on nowadays in every audiological laboratory. In these tests *there are purely technical difficulties and sources of* error which one must be aware of and constantly guard against.

So far as tone audiometry *is concerned*, one should bear in mind the following:

In the usual method with an external receiver (headphone) assuming that no cross masking is present a conductive loss can amount at most to 60 db With greater losses than 60 db the excess loss can be regarded as sensori neural Thus with the usual methods the difference between the air and bone conduction curves should not exceed 60 db

The bone conduction curve as a rule gives an estimate of sensori neural function On the other hand a lowered bone conduction curve does not necessarily point to cochlear degeneration In otosclerosis for example we usually distinguish among four different causes of reduced bone conduction

1 Stapes fixation is accompanied by a change in transmission which leads to a certain lowering of the bone conduction curve the so called Carhart notch This is not a sign of cochlear degeneration since the bone conduction curve becomes normal after operation The depth of the Carhart notch is 5 10 15 and 5 db for the frequencies 500 1000 2000 and 4000 Hz One should of course remember that these figures are average values with considerable individual variation for which reason individual losses of as much as 30 db at single frequencies may occur even though cochlear function is normal

By correcting the bone conduction curve with the above values for the Carhart notch one gets an approximate measure of actual cochlear function

2 Extreme lowering of the bone conduction curve can point to the occlusion of the round as well as the oval window If the speech audiogram shows normal discrimination values and the difference limen according to the Bekesy audiogram is normal the lowered bone conduction curve can be an expression of reduced transmission in the inner ear caused by the occlusion of both windows

3 With reduced discrimination and smaller difference limen the impaired bone conduction is on the contrary an expression of deteriorated cochlear function

4 The fourth case of reduced bone conduction values is artificial and is due to incorrect calibration or to the use of an excessive intensity of masking Bone conduction measurements are well known to be characterized by great uncertainty This uncertainty depends upon a number of factors such as difficult calibration variable placement of the bone receiver and inadequate receivers

If there is reason to suspect that the bone conduction measurement is incorrect the following should be checked

1 Weber and Rinne tests

2 The *speech audiogram* is a sensitive indicator of cochlear function Reduced *discrimination* capacity clearly indicates a sensori neural defect

3 The *occlusion test* shows in cases of sensori neural loss an improvement of bone conduction at frequencies below 1000 Hz

4 *Impedance measurement* of the stapedius reflex can help to decide whether it is a case of sensori neural or conductive defect

Special Tests

For the topical diagnosis of conductive defects a number of audiological tests are now available some of which have achieved widespread distribution while others are as yet carried out only in the best equipped audiological laboratories All of them provide various ways of analysing the cause of conductive defects The result of a single special test rarely gives the whole truth whereas the combined answer from several different tests gives considerably more reliable information

Sound transmission in the normal ear takes place via the eardrum ossicular chain and oval window to the inner ear The most important task of the middle ear is to compensate for the loss of about 30 db which otherwise would occur when the sound waves are transmitted from the air to the fluid in the inner ear Because of the difference in area between the eardrum and the oval window and to a lesser degree because of the mechanical advantage of the ossicular chain the sound intensity at the eardrum is increased about 22 fold which corresponds to approximately +27 db In other words if one applies the sound through a tube directly and exclusively to the oval window by passing the middle ear one gets a hearing loss of about 27 db varying somewhat at different frequencies

The amplifying effect of the middle ear decreases with pathological changes in the eardrum and ossicles As long as the latter and the windows are functioning quite normally a reduction of the eardrum s vibratory surface has a relatively slight effect on the hearing If the perforation is so great that only a tenth of the eardrum s surface remains the hearing loss at least in theory is no greater than 26 db

When the sound waves reach the inner ear via the oval window they give rise to an inward traveling wave The condition for optimal stimulation of the organ of Corti is that the inward pressure of the stapes produces a reciprocal outward bulging of the round window membrane and vice versa Normally this movement is countered to some extent by sound waves striking the round window at the same time by way of the air in the middle ear Since the drum membrane opposes the direct passage of sound from the external canal to the round window it reduces this interference by its so called sound protective effect If the drum is thin and atrophic or if it is perforated its sound protective effect is diminished

The sound transforming effect predominates over the sound protective effect and even large perforations cause only trifling hearing loss provided the ossicles are functioning In the case of smaller perforations their position also plays a certain role If the perforation lies directly over the round window the hearing loss is greater than if it lies in the anterior quadrant In the latter case the round window is still protected by the remaining portion of the drum membrane

In the case of window hearers where eardrum malleus and incus are missing one gets theoretically a hearing loss of 40 45 db if the windows are

quite normal With scarring e g after radical operations, it is not unusual to find hearing losses as great as 60 db

The prosthesis test has been known and used for a long time Assuming that the prosthesis is placed by an experienced hand with the aid of the micro scope either an improvement of hearing or a lack of improvement can give valuable information On the other hand an incorrectly placed prosthesis can give definitely misleading information The air conduction audiogram is taken before and after the introduction of the prosthesis If the air conduction curve with the help of the prosthesis comes up from 30 db to the 10–20 db level (according to European standard) the ossicles and windows are func tioning normally and no sign of obstructive adhesive process is likely to be present Parenthetically it may be pointed out here that there is no reason to suspect an interruption of the ossicular chain if the pure tone audiogram does not lie above the 30 db level An exception to this rule occurs if on examina tion one can see that a portion of the eardrum is adherent to the stapes and a natural myringo stapediopexy has arisen From a surgical point of view however, this situation can be placed in the same category as a functioning ossicular chain When the hearing loss amounts to 45 db an increased im pedance is present in the ossicles If the prosthesis test shows unchanged or deteriorated hearing there is either a break in the ossicular chain, adhesions in the atticus or fixation of the stapes By pressing the prosthesis in against the stapes one can get a hint as to which of these conditions is present With an interruption of the ossicular chain but with normal stapedial mobility we get an improvement in hearing whereas with stapes fixation the hearing curve remains unchanged

Sound probe measurement is the determination of the threshold for tones by means of a sound probe at different points in the ear With a normal ossi cular chain one finds a difference of 40–50 db when the probe is placed on the wall of the auditory canal and on the shaft of the malleus respectively With a break in the ossicular chain this difference is small or absent With an increased impedance caused by adhesions in the ossicular chain or otosclerosis one gets 20 to 30 db lower thresholds on the shaft of the malleus than on the wall of the auditory canal

The mobility of the eardrum which is a good indication of the condition of the middle ear can be judged by *tympanometry* When one measures the relative impedance of the eardrum with pressure variation in the auditory canal one normally gets a V shaped curve With negative pressure in the middle ear the minimum of the curve is shifted in the negative direction With adhesions or effusion in the middle ear the curve becomes a straight line With a break in the ossicular chain it often resembles a W

Evoking the tensor tympani reflex by means of a jet of air in the eye and registering by the impedance method is useful especially when a break in the ossicular chain is suspected With such an interruption the eardrum is as a rule abnormally mobile and one gets a greater reflex response

In hearing losses of obscure nature the *occlusion test* can be useful The

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In the case of window hearers, where eardrum malleus and incus are missing one gets theoretically a hearing loss of 40–45 db if the windows are

4 *Are there any morphological or functional defects in the eardrum or ossicles?*

When one tries to find the cause of an increased impedance in the middle ear one must differentiate between cases with an intact eardrum and those with a perforation

If the eardrum is intact there are three main differential diagnostic possibilities The commonest cause of increased impedance is *otosclerosis* Here the normal appearance upon microscopic examination normal tubal function together with the audiometric data give a probable diagnosis An apparently normal eardrum can also be present in patients with a *break in the ossicular chain* even though it is far more common for the cause of such a break to have left its mark on the eardrum as well In such cases the differential diagnosis ruling out otosclerosis may be difficult to make A case history of sudden loss of hearing associated with trauma an audiogram which shows a conductive hearing loss of 60 db a sound probe test showing a trifling difference or none between the auditory canal and the shaft of the malleus a double peak in the tympanometric curve and strong responses in measurement of the tensor reflex all these furnish good bases for making the diagnosis The third differential diagnostic possibility is *adhesive otitis* For these cases an ordinary eardrum examination and especially microscopic examination give a good basis for the diagnosis In certain cases however adhesive otitis can show an eardrum in normal position with the middle ear filled by a fibrotic mass In these patients however one finds neither eardrum mobility nor tubal function furthermore the eardrum is usually indurated and fibrotic

In a patient with a perforation of the drum the increased impedance in the middle ear may be caused either by the perforation itself or by the perforation plus changes in the ossicular chain or oval window In most cases a careful preoperative investigation will clarify the situation Microscopic examination with palpation of the various parts of the ossicular chain sound probe measurement and the prosthesis test usually give all the information necessary

5 *How well are the oval and round windows functioning?*

Tone and speech audiometry prosthesis and sound probe tests give in general a satisfactory answer Supplementary information can be obtained by microscopic examination of the round window niche after filling it with fluid When the ossicles are palpated with a small probe one sees if the windows are functioning normally a movement of the light reflex

In cases where the stapes is visible one can determine the mobility of the stapes by clapping the hands and thus eliciting the stapedius reflex If the footplate is normally mobile the reflex movement will be clearly seen

bone conduction is tested with and without occlusion of the auditory canal of the actual ear. If the bone conduction under 1000 Hz is improved by occlusion, a sensori-neural defect is indicated. If it remains unchanged the defect is conductive

The demonstration of the *stapedius reflex* by the impedance method is used not only as a recruitment test, but also for differential diagnosis between conduction and sensori-neural defects It can with good reason be said that, if the reflex can be demonstrated, the middle ear is functioning normally This means that if hearing loss is present it is of sensori-neural origin

DISCUSSION OF THE CASE

The aim of the preoperative investigation is to collect a sufficient number of facts and with their help to try in turn to answer the questions posed in the introduction

1 *How great a handicap is the patient's hearing loss?*

The routine examination with tone and speech audiometry gives a picture of what the hearing loss means to the patient, in terms of increased difficulty in communicating with his surroundings As stated earlier, however, this question is not completely answered until the patient's audiometric hearing loss has, so to say, been placed in its right setting, i e his situation in life Not until then has one an adequate basis for assessing the degree of motivation for an operation to improve his hearing

2 *Is there any active infection, irritation or cholesteatoma present, which can prevent an operation from improving the hearing?*

The answer to this question is of great importance because it weighs heavily in the further handling of the case Although the question is easily answered when it is a matter of nasty, infected ear or a dry irritation free ear, it is difficult to judge the finer shades between these two extreme pictures A careful case history and physical examination, a microscopic examination and X ray examination give a good lead, but only the experienced otologist is able to make an adequate synthesis of these data

3 *How well are the Eustachian tubes functioning?*

By means of the tubal function tests referred to above, it is possible to ascertain whether the tubal passage is normal reduced or abolished To a certain extent we can also get a quantitative idea of the degree of loss of function in the tube Unfortunately, we do not know how great a loss of tubal function can be permitted without constituting a contraindication for a tympanoplastic operation

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By means of the tubal function tests referred to above it is possible to ascertain whether the tubal passage is normal, reduced or abolished. To a certain extent we can also get a quantitative idea of the degree of loss of function in the tube. Unfortunately we do not know how great a loss of tubal function can be permitted without constituting a contraindication for a tympanoplastic operation.

the stapedius muscle is disturbed which carries a greater risk of noise injury and an undesirable increase in loudness for the lower frequencies The risks involved also contraindicate operation above all the risk of cochlear injury Such injury always means a greater handicap for the patient in the form of impaired speech communication especially in noisy surroundings Besides this injury is considerably more difficult to compensate for with a hearing aid than a conductive loss Therefore the risk of injury must not be ignored even if the injury is not severe In summary, the thresholds for speech in quiet and noisy surroundings the discrimination score and the patient s situation in life constitute the most important basis for the decision whether to recommend otosclerosis surgery for a patient with an average air-bone gap of *less* than 40 db Tests made in the artificially quiet atmosphere of an audiometer room are not a sufficient indication for operation in cases of this type

2 *Interruption of the ossicular chain*

Assuming that cochlear function is satisfactory an exploratory tympanotomy with an attempt to restore the continuity of the chain is indicated in all cases with a break in the ossicular chain

3 *Adhesive otitis*

In the *majority* of such patients tubal insufficiency forms the pathophysiological basis for an adhesive process in the middle ear Only in exceptional cases can an operation improve the function of the tube The indications for operation in adhesive otitis must therefore be regarded as very limited

C *Patients with perforated eardrum*

1 Cases of *central perforation* with the middle ear functioning normally should undergo myringo-plastic surgery partly to improve the hearing and partly as a protection against external infections

2 Cases of central perforation and involvement of the ossicles should have a *myringo* plastic operation with measures taken to restore sound transmission In cases of perforation together with stapes fixation myringo plasty is *followed* with stapes surgery at a later time

3 Patients who lack eardrum and ossicles may in certain cases be operated with a so *called* cavum minor operation

4 Patients with marginal perforation should be explored and cleaned up before closing With regard to the treatment of these cases the reader is referred to paragraph 4 above

ZUSAMMENFASSUNG

Bei der praoperativen *Beurteilung* von Gehörschaden ist es zu empfehlen folgende Fragen zu beachten Der *Grad* der Invalidität des Patienten auf Grund des Gehörschadens sind Zeichen für eventuelle Infektionen Irritation oder Cholesteatom

6 *How is the sensori neural function?*

The gap between the air and bone conduction curves in the pure tone audiogram sets the theoretical limits for improvement of hearing It is therefore of the greatest importance that the audiometric diagnosis reflects reality and nothing else With the knowledge of the purely technical difficulty that can arise one should constantly be on guard against errors of audiometric measurement and carefully weigh the other findings in the preoperative investigation against the audiogram itself

7 *Are there indications for operation present?*

Having tried to answer the foregoing questions as completely as possible in the preoperative investigation one must decide how to handle the case Three choices present themselves to avoid surgery altogether to perform surgery of infections of the ear or to perform an operation to improve the hearing The many factors which affect this decision vary from case to case and only basic guidelines can be drawn up here

A In cases of active infection irritation cholesteatoma or reduced tubal function there are relative to absolute contraindications against tympanoplastic operation depending upon the degree of change In the first place conservative therapy is tried including general or local treatment with antibiotics and possibly antiallergic treatment In doubtful cases one can try covering the perforation with an eardrum prosthesis If the prosthesis remains in place the conditions for a tympanoplastic operation can be considered favourable If one cannot succeed with conservative therapy one should always choose first an operation for the infection of the ear

B In cases with intact eardrums the preoperative investigation gives three differential diagnostic possibilities

1 *Otosclerosis*

When the gap between the average threshold for air and bone conduction for frequencies of 500 1000 2000 Hz exceeds 40 db an operation is well justified

When the gap is less marked a more careful analysis must be made before the patient is advised to have an operation Deciding on the basis of the pure tone audiogram alone can be misleading It is not unusual for a patient with a rising curve to have a gap greater than 40 db for low frequencies but only 10 15 db at 2000 Hz The pure tone audiogram for such a patient tempts one to operate whereas the speech audiogram shows that the patient has only a very slightly raised threshold because of the greater information content of the higher speech frequencies It is doubtful therefore whether a patient with this type of hearing loss has anything to gain by an operation Speech communication will remain unchanged or may possibly be a little better in quiet surroundings but it will be worse in noisy surroundings The action of

A STUDY OF CONGENITAL NYSTAGMUS

B. FORSSMAN,
Lund, Sweden

From the Department of Neurology (Acting Head: Doc. O. Berg) and from the Department of Otolaryngology (Head: Prof. Hj. Koch), University of Lund

Ninety cases of congenital idiopathic nystagmus were examined by ophthalmologists and by the author, chiefly electrooculographically. The results of these examinations were:

The visual acuity of the better eye was normal or almost normal in largely 1/3 of the cases, and the refractive errors of the better eye were absent or small in 1/2 of the cases. Squint was present in 16 per cent.

The neutral zone for regular pendular eye movements had an eccentric position in 35 per cent to such a degree that turning of the head on fixation ensued.

The nystagmus in darkness, as compared to light, was almost always suppressed when the eyes were closed but presented a quite different pattern when the eyes were open, showing decrease in 33, increase in 7 and no decided or variable changes in 60 per cent.

Mephenesin depressed the spontaneous nystagmus in 1/3 of the cases and caused a significant decrease of calorically induced nystagmus.

The vestibulo-ocular reactivity was undecided in 10, normal in 46 and absent in 44 per cent of the cases. The audiograms were essentially normal. Vestibulo-ocular areflexia was presumed to be caused by central influence.

INTRODUCTION

Congenital nystagmus is defined as nystagmus of a pendular type existing from birth or early infancy. It comprises two groups: the ocular and the idiopathic.

Cases of congenital ocular nystagmus differ by the presence of gross congenital ocular defects (e.g. aniridia, microphthalmia, opacities of the media, albinism) from congenital idiopathic nystagmus.

The present investigation is concerned only with the idiopathic group, briefly called congenital nystagmus.

The factors relevant in a discussion of the disease are as follows:

The disease is relatively rare (one case out of 6500 inhabitants according to Rempies 1924), more common in males than in females.

The formal genesis is unknown. Not infrequently the causal genesis has been shown to be of hereditary nature. Three types of inheritance have been distinguished: irregular dominant, recessive sex-linked, and simple recessive

This investigation was supported by the Medical Faculty, University of Lund.

vorhanden, welche eine gehorverbessernde Operation ungunstig beeinflussen konnen? Ist die Funktion der Tuba-Eustachi normal? Konnen funktionelle oder morphologische Defekte des Trommelfelles oder der Gehörknochen festgestellt werden? Wie ist die Funktion des runden und ovalen Fensters? Wie ist die Funktion des Innenohres? Kann eine Operation befurwortet werden?

Die praoperative Beurteilung des Falles umfasst eine klinische, rontgenologische und audiologische Untersuchung und ausserdem eine Besprechung des Falles

Dept of Otolaryngology Sahlgrenska Hospital
Göteborg Sweden

Received May 15, 1963

A STUDY OF CONGENITAL NYSTAGMUS

B Forssman
Lund Sweden

From the Department of Neurology (Acting Head Doc O Berg) and from the Department of Otolaryngology (Head Prof Hj Koch) University of Lund

Ninety cases of congenital idiopathic nystagmus were examined by ophthalmologists and by the author chiefly electrooculographically The results of these examinations were

The visual acuity of the better eye was normal or almost normal in largely 1 3 of the cases and the refractive errors of the better eye were absent or small in 1 2 of the cases Squint was present in 16 per cent

The neutral zone for regular pendular eye movements had an eccentric position in 35 per cent to such a degree that turning of the head on fixation ensued

The nystagmus in darkness as compared to light was almost always suppressed when the eyes were closed but presented a quite different pattern when the eyes were open showing decrease in 33 increase in 7 and no decided or variable changes in 60 per cent

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Persistence from birth or early infancy of pendular nystagmus according to the definition. The eye-movements are almost always horizontal

Errors of refraction are common, as is also squint Visual acuity is sometimes normal but most often lowered, though seldom to any great extent The fundi are normal although the pigmentation may be reduced

The patients have no *sensation of oscillopsia* unless tired or emotionally upset, when there is an augmentation of the eye-movements

The nystagmus generally increases on fixation and decreases on absence of fixation. The movements of the eyes are pendular in a neutral zone Usually they increase on lateral gaze from this zone and then often change to a jerky type with the fast component in the direction of the gaze When the neutral *zone has an eccentric position in relation to the median plane of the head* the patient on fixation usually turns his head to the side of the fast component of the nystagmus and the eyes compensatorily in the opposite direction, thus bringing them into the neutral zone in front of the body.

Shaking of the head is rare.

In a few cases the vestibulo-ocular reflexes have been found *to be diminished* or lost.

Aim of the investigation

The present work is mainly an electrooculographic examination of the following principal points

(1) Above all the vestibulo-ocular reflexes, but also

(2) The differences in nystagmus between light and darkness, and

(3) The influence of mephenesin on the nystagmus

A report of the *ophthalmological state of congenital nystagmus* will also be given

History

1) Reports on ophthalmological disturbances in congenital nystagmus have usually been vague or based on small materials

Visual acuity has most often been found to be moderately decreased Thus Rucker (1946) reported most values to be of the order 0 7 0 4, but did not give the number of examined cases Hemmes (1924) median value of the visual acuity of 40 eyes was 0 3 with correcting glasses *the highest value being* 0 9. Cuendet & della Porta (1949) found a range between 0 8 and 0 1 in 25 cases Anderson (1953) reported a variation between 1 0 and less than 0 1 among 85 cases, which, however, also included the ocular group of congenital nystagmus

The most *comprehensive study has been reported by* Gamble (1934) Among 65 cases the visual acuity of the better eye with correcting lenses was 1 5 0 7 in 27 cases (42 %), 0 6 0 4 in 25 cases (38 %) and 0 3 0 1 in 13 cases (20 %)

Refractive errors Astigmatism was noted by Cuendet & della Porta (1949) in all their 25 cases and by Kaser (1942) in 6 of his 13 cases

Nettleship (1911) reported that out of 56 cases 6 had emmetropia (11 %) 9 hyperopia (16 %) 24 hyperopia and astigmatism (43 %) 4 myopia (7 %) 5 myopia and astigmatism (9 %) 3 mixed astigmatism (5 %) 1 a slight astigmatism (2 %) while 4 were undecided (7 %)

Among 130 eyes (65 cases) Gamble (1934) found 10 to be emmetropic (8 %) 102 to be hyperopic (78 %) and 18 to be myopic (14 %) The average spherical error in hyperopes was +2 74 D and in myopes —3 52 D Of the 130 eyes 12 were without astigmatic errors (9 %) and 118 had such errors (91 %) The average astigmatic error was 1 38 D

Squint has not infrequently been reported

Gamble (1934) noted 26 such cases in his material of 65 persons (40 %)

2) *Changes in congenital nystagmus between light and darkness* Since the introduction of electrooculography it has been possible to compare the behaviour of nystagmus in light with that in darkness Most authors have studied the eye movements in darkness by making the patients close their eyes in a lighted room while some make them open their eyes in complete darkness

Congenital nystagmus in light is said nearly always to be suppressed often completely when the eyes are closed (Aschan & Bergstedt 1955 Aschan Bergstedt & Stahle 1956 Catalano & Madonia 1957 Motta von Berger & Baravelli 1957 Blomberg 1959 Suzuki 1961) Aschan & Bergstedt (1955) however noted exceptions to this general rule in two cases the ocular movements were only insignificantly affected by eye closure and in one case the nystagmus curve was only qualitatively but not quantitatively changed by the same procedure

Motta von Berger & Baravelli (1957) found about the same depressive effect on the congenital nystagmus by closing the eyes as by keeping them open and turning off the light Suzuki (1961) reported that the increase of pendular nystagmus is about the same when a patient opens his eyes in darkness as in light

The eye movements often decrease when a patient with congenital nystagmus fixes a near by object (Nettleship 1911 Kaser 1942)

In this connection may be mentioned the interesting experiments of Desschate (1952 1954) on normal persons He showed that pendular nystagmus frequently arose when light reached the retina and the stimulus for the fixation mechanism was abolished

3) *Influence on congenital nystagmus by drugs* It is known that promethazine hydrochloride B P (Lergigan ®) decreases or abolishes calorically induced nystagmus in normals (Blomberg 1956) and that barbiturates cause resp increase gaze nystagmus in normals and especially in cases of brain damage (Bender & O Brien 1946 Bergman Nathanson & Bender 1951 1952 Bender Nathanson & Green 1951 Blomberg 1955 1957 1958)

In cases of congenital nystagmus amobarbital U S P (Pentymal ®)

decreases the pendular eye movements in front and increases them on lateral gaze (Bender & O'Brien, 1946, Bergman, Nathanson & Bender 1951, 1952).

Mephenesin N.F. ("Myanesin"®) has the same effect on congenital nystagmus as amobarbital though it is not so regular (Bender & O'Brien 1946, Bergman, Nathanson & Bender, 1951, 1952). Suppression of congenital nystagmus from mephenesin was also noted by Felisati & Fregni (1953) and by Menna (1956).

According to Cuendet & della Porta (1949) alcohol increases congenital nystagmus.

f) *The vestibular reactivity in congenital nystagmus.* In 1921 Brunner reported abnormalities of the vestibular reactivity in three cases of pendular nystagmus.

Case 1. On calorizations no nystagmus reactions but almost normal vertigo. On rotations normal nystagmus reactions and vertigo. Case 2. On calorizations and rotations no nystagmus reactions and no vertigo. Case 3. On calorizations weak nystagmus reactions but no vertigo. On rotations no nystagmus reactions and no vertigo.

Sommer (1921) stated as a general rule that calorically induced nystagmus reactions were difficult to evoke in cases of pendular nystagmus.

Hemmes (1921) found abnormal vestibulo-ocular reflexes among 6 cases of congenital nystagmus examined by cold calorization.

One case showed no nystagmus reaction on either side, two cases no reactions on one side and weak reactions on the other, and two cases no reactions on one side and normal ones on the other. One case was irrigated only on one side and showed no reaction.

Forsythe (1955) found no nystagmus reactions in a case of congenital nystagmus irrigated with water of 30° and 44° C in each ear.

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His findings are not in line with the general view that vestibularly induced nystagmus is more pronounced in darkness than in light. The suppressive effect of eye closure on nystagmus is usually not so pronounced that it could conceivably explain his results.

When combining two forms of nystagmus, both of vestibular origin (e.g. a spontaneous and an induced one), no superposition of the two occurs but the existing nystagmus is increased or decreased according to the second one beating in the same or in the opposite direction. When combining a non-vestibular form of nystagmus with a vestibular one the two forms of nystag-

mus are possible to discern the one being superimposed on the other.—This has been proved by de Kleyn (1939, 1949) and by Aschan & Bergstedt (1955).

5) *The cause of congenital nystagmus* is unknown. The generation of congenital as well as other forms of nystagmus must of course occur in the central nervous system. Opinion, however, is divided as to the question if nystagmus is peripherally (eyes, possibly labyrinth) released or not.

Hemmes (1924) arrived at the assumption, adopted by no other author, that nystagmus is due to a reduced function of the otolith mechanism.

Many authors consider nystagmus to be released from the eyes (cf. Kestenbaum 1948, Aschan & Bergstedt 1955, Motta, von Berger & Baravelli 1957). Their conception is based on the findings that (a) nystagmus is more prominent in light than in darkness and that (b) the persons with congenital nystagmus have often ophthalmological disorders such as decreased visual acuity and refractive errors. When such ophthalmological disturbances are present during the first four months of life that only blurred contours are projected on the retina, the macula does not develop in the ordinary way and the fixation mechanism cannot function properly in the future.

Objections to this conception have been raised by many authors. (a) Thus nystagmus often does not disappear completely in darkness and in some cases is not even reduced at all. (b) Not infrequently there are also cases of congenital nystagmus with no ophthalmological disorders. In such cases, however, there might have been pronounced refractive errors during the first four critical months of life. (c) Cases are known of pendular eye movements existing from the day of birth or from the first few days of life when the macula is undeveloped (Owen 1882, Hawthorne 1903, Nettleship 1911, Rucker 1946, Forsythe 1955).

Whatever the formal genesis may be, the causal genesis is not infrequently of an hereditary nature.

MATERIAL

The material was largely collected via records from experts on ophthalmological diseases, mainly those of the University Eye Clinic in Lund. A few cases were discovered in other ways.

The following cases were omitted from the examination:

(1) Those with a visual acuity of less than 0.1 on either eye without correcting lenses. *In these cases the tests for electrooculography would probably have been difficult to perform.* Persons omitted for this reason were few in number.

(2) Children younger than 11 years of age.

(3) Patients living far away from Lund.

Otherwise the material was unselected. The material comprised 61 men aged 11–57 years and 29 women aged 13–60 years, i.e. a total number of 90 cases 11–60 years of age.

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the fast component which can be excluded from the derived tracing down wards

Calibrations of the amplitude tracing (lower curve) were performed by having the patient look alternatively between two white marks 20 degrees apart and those of the velocity tracing (upper curve) by making the patient pursue vertical stripes of light moving at 20 degrees per second on the inside of a surrounding drum

Caloric irrigations with the patient in a supine position and his eyes open were performed during 40 seconds in complete darkness The right ear was first irrigated with water of 30°C and then the left These irrigations were as a rule repeated after administration of mephenesin (see below) In a few instances the patients were also irrigated with water of 44°C in the right and left ear In cases where no jerky nystagmus appeared from calorizations with water of 30°C irrigations with ice water on the right and left side were also *not seldom performed* Instead of using ice water double irrigations were sometimes performed For example the right ear was then irrigated with water of 30°C and simultaneously the left ear with water of 44°C

Rotational examinations were performed using the technique of Henriksson (1956) The patient was sitting in a comfortable dentist s chair The rotations were performed in complete darkness with the patient s eyes open By falling weights the chair was brought to accelerate from standstill until one turn had been covered The angular velocity of the chair was recorded on the lower tracing of the Mingograph The time for acceleration was usually a little shorter than that for deceleration Because the weights of the patients differed the accelerations differed also The mean value for acceleration was 12 7°/sec^2 and for the angular velocity at the end of acceleration 90 0°/sec

Mephenesin was given to most of the patients As the intravenous administration may cause *complications* (e g thrombophlebitis renal damage) the oral route was preferred Because the pellets were relatively ineffective and *because* the commercial solution contains alcohol which might influence *the* nystagmus a special solution was given Mephenesin 6 6 g Propylenglycoll 40 g Aq dest ad 100 g The dose administered was 20 mg/kg body weight

The scheme for examination in the vestibular laboratory was generally as follows (all *the time* with registration of the eye movements)

Sitting *position* —Light Binocular fixation in front and 20 degrees to the right and *left* Monocular fixation *in front* with the right and the left eye Fixing an object at *distances of* 40 30 and 20 centimetres from the eyes Alternating periods of light and darkness with the patient gazing in front and closing his eyes *in darkness* for a short while when being told so —Rotation in darkness to the right and to the left sometimes repeated

Supine *position* in darkness Head in front position and *turned to the right* and left Calorization first of the right then of the left ear with water of 30°C

The patient was then given mephenesin and from half an hour thereafter the above ... epeated

All these had been told that their nystagmus had been present since early infancy In four cases the mothers interviewed by the author were quite sure that the nystagmus existed already from the day of birth

Examinations

The study comprised case histories neurological and ophthalmological examinations audiometry and electronystagmographic recordings of the spontaneous eye movements and of the vestibular reactions

Apart from the nystagmus and the state of the eyes 86 of the cases were healthy and four suffered from the following diseases

Case no 5 ♂ 24 years old Bonnevier Ulrich s disease Klippel Feil s syndrome and spina bifida occulta

Case no 77 ♂ 40 years old After a head injury at 34 years of age he has suffered from a postconcussion syndrome and 2 years later also from epilepsia interpreted as a complication of the trauma

Case no 89 ♀ 35 years old Debility Since 22 years of age periods of psychic insufficiency and increasing hearing loss probably of hereditary nature

Case no 91 ♂ 11 years old Debility Cerebral atrophy according to pneumoencephalography

Neurological examinations of all cases were normal except absence of muscle stretch reflexes in the legs and weak ones in the arms in case no 89

The eyes of all cases were examined by specialists on ophthalmological diseases

In 85 cases pure tone audiograms were performed In 2 of these cases speech audiograms were also accomplished

The electronystagmographic recordings of the spontaneous eye movements and of the vestibular reactions will be considered specially

METHODS

Nystagmus was recorded by the electrooculographic method introduced by Henriksson (1955 1956) The potential differences between the temples from eye movements passed through an amplifier and were registered on a two channel ink writing recorder (Mingograph AB Elema Stockholm)

The lower channel was used for the conventional nystagmus curve where the deflexions are directly proportional to the amplitude of the eye movements In rotational experiments this channel was instead used for recording the angular velocity

The upper channel was used for the derived tracing where the deflexions were directly proportional to the velocity of the eye movements

The deflexions upwards in both curves represented eye movements to the right and those downwards to the left In vestibular stimulations the polarity of the electrical circuit was so selected that the expected slow component of caloric and perrotatory nystagmus was recorded as deflexions upwards and

the fast component which can be excluded from the derived tracing downwards

Calibrations of the amplitude tracing (lower curve) were performed by having the patient look alternatively between two white marks 20 degrees apart and those of the velocity tracing (upper curve) by making the patient pursue vertical stripes of light moving at 20 degrees per second on the inside of a surrounding drum

Caloric irrigations with the patient in a supine position and his eyes open were performed during 40 seconds in complete darkness The right ear was first irrigated with water of 30°C and then the left These irrigations were as a rule repeated after administration of mephenesin (see below) In a few instances the patients were also irrigated with water of 44°C in the right and left ear In cases where no jerky nystagmus appeared from calorizations with water of 30°C irrigations with ice water on the right and left side were also not seldom performed Instead of using ice water double irrigations were sometimes performed For example the right ear was then irrigated with water of 30 C and simultaneously the left ear with water of 44°C

Rotational examinations were performed using the technique of Henriksson (1956) The patient was sitting in a comfortable dentist s chair The rotations were performed in complete darkness with the patient s eyes open By falling weights the chair was brought to accelerate from standstill until one turn had been covered The angular velocity of the chair was recorded on the lower tracing of the Mingograph The time for acceleration was usually a little shorter than that for deceleration Because the weights of the patients differed the accelerations differed also The mean value for acceleration was 12 7°/sec² and for the angular velocity at the end of acceleration 90 0°/sec

Mephenesin was given to most of the patients As the intravenous administration may cause complications (e g thrombophlebitis renal damage) the oral route was preferred Because the pellets were relatively ineffective and because the commercial solution contains alcohol which might influence the nystagmus a special solution was given Mephenesin 6 6 g Propylenglycoll 40 g Aq dest ad 100 g The dose administered was 20 mg/kg body weight

The scheme for examination in the vestibular laboratory was generally as follows (all the time with registration of the eye movements)

Sitting position —Light Binocular fixation in front and 20 degrees to the right and left Monocular fixation in front with the right and the left eye Fixing an object at distances of 40 30 and 20 centimetres from the eyes —Alternating periods of light and darkness with the patient gazing in front and closing his eyes in darkness for a short while when being told so —Rotation in darkness to the right and to the left sometimes repeated

Supine position in darkness Head in front position and turned to the right and left Calorization first of the right then of the left ear with water of 30°C

The patient was then given mephenesin and from half an hour thereafter the above procedures were repeated

All these had been told that their nystagmus had been present since early infancy In four cases the mothers, interviewed by the author, were quite sure that the nystagmus existed already from the day of birth

Examinations

The study comprised case histories, neurological and ophthalmological examinations, audiometry and electronystagmographic recordings of the spontaneous eye-movements and of the vestibular reactions

Apart from the nystagmus and the state of the eyes, 86 of the cases were healthy and four suffered from the following diseases

Case no 5 ♂ 24 years old Bonnevier-Ulrich's disease, Klippel Feil's syndrome and spina bifida occulta

Case no. 77 ♂ 40 years old After a head injury at 34 years of age he has suffered from a postconcussion syndrome and 2 years later also from epilepsia, interpreted as a complication of the trauma

Case no 89 ♀ 35 years old Debility. Since 22 years of age periods of psychic insufficiency and increasing hearing loss, probably of hereditary nature

Case no 91 ♂ 11 years old Debility Cerebral atrophy according to pneumoencephalography

Neurological examinations of all cases were normal except absence of muscle stretch reflexes in the legs and weak ones in the arms in case no 89

The eyes of all cases were examined by specialists on ophthalmological diseases

In 85 cases pure tone audiograms were performed In 2 of these cases speech audiograms were also accomplished

The electronystagmographic recordings of the spontaneous eye movements and of the vestibular reactions will be considered specially

METHODS

Nystagmus was recorded by the electrooculographic method introduced by Henriksson (1955, 1956) The potential differences between the temples from eye movements passed through an amplifier and were registered on a two channel inkwriting recorder (Mingograph AB Elema, Stockholm)

The lower channel was used for the conventional nystagmus curve, where the deflexions are directly proportional to the amplitude of the eye movements In rotational experiments this channel was instead used for recording the angular velocity

The upper channel was used for the derived tracing where the deflexions were directly proportional to the velocity of the eye movements

The deflexions upwards in both curves represented eye movements to the right and those downwards to the left In vestibular stimulations the polarity of the electrical circuit was so selected that the expected slow component of caloric and perrotatory nystagmus was recorded as deflexions upwards and

the fast component which can be excluded from the derived tracing downwards

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The visual acuity was tested at the beginning of the examination and about 25 minutes after the administration of mephenesin.

Statistical terminology: A difference was said to be significant*, significant**, or significant*** when the corresponding P-value was equal to or less than 5, 1, or 0.1 per cent, respectively. When P was greater than 5 per cent, the difference was regarded as not significant.

RESULTS

A. *Ophthalmological examinations*

The ophthalmological examinations were performed by experts on ophthalmological diseases.

The four cases with congenital nystagmus also suffering from other diseases have been omitted from the following survey.

Corrected visual acuity at the last examination, determined on each eye according to Monoyer, has been divided into three groups: 1.0–0.7, 0.6–0.4, and 0.3–0.1. When the two eyes of the same patient belonged to the same group, the one eye has been referred to "better eye" and the other to "worse eye", see table 1.

TABLE 1. *Corrected visual acuity of 86 cases of congenital nystagmus*

Visual acuity	Better eye: No. of cases	Better eye: %	Worse eye: No. of cases	Worse eye: %
1.0–0.7	32	37	24	28
0.6–0.4	38	44	29	34
0.3–0.1	16	19	33	38

Refractive errors. The distribution of the different kinds of refractive errors irrespectively of the degree was as follows:

	Number of cases	Per cent
Emmetropia and uncorrected slight ametropia	12	14
Corrected ametropia		
Myopia	6	7
Hyperopia	7	8
Astigmatism	15	17
Myopic astigmatism	22	26
Hyperopic astigmatism	24	28

The degree of refractive errors, determined on each eye usually by skiascopy, has also been divided into three groups:

TABLE 2 *Refractive errors of 86 cases of congenital nystagmus*

Abbreviations see text

Refractive errors	Better eye No of cases	Better eye %	Worse eye No of cases	Worse eye %
H or M ≤ 2 D and or As ≤ 1 25 D	43	0	33	38
2 D < H or M ≤ 6 D and or 1 25 D < As ≤ 2 5 D	30	35	35	41
6 D < H or M and or 2 5 D < As	13	15	18	21

(1) Hyperopia or myopia equal to or less than 2 D and/or astigmatism equal to or less than 1 25 D (abbreviated H or M ≤ 2 D and/or As ≤ 1 25 D)

(2) Hyperopia or myopia more than 2 D but less than or equal to 6 D and/or astigmatism more than 1 25 D but less than or equal to 2 5 D (abbreviated 2 D < H or M ≤ 6 D and/or 1 25 < As ≤ 2 5 D)

(3) Hyperopia or myopia more than 6 D and/or astigmatism more than 2 5 D (abbreviated 6 D < H or M and/or 2 5 < As)

When the two eyes of the same patient belong to the same group one eye has been referred to better eye and the other to worse eye see table 2

Changes as in high myopia were not found in any eye

Squint was found in 14 of the 86 cases (16 per cent)

Pigmentation of the fundus was noted to be slightly subnormal in 15 cases (17 per cent) Higher grades of depigmentation were never seen

Comments The ophthalmological disturbances are in excess of normality As far as visual acuity is concerned this is clearly evident From frequency distribution reports (cf Scheerer 1928 Betsch 1929 Brown & Kronfeld 1939 Duke Elder 1949) the refractive errors are also found to be more common in cases with congenital nystagmus than in the general population The same is true of squint (normal frequency in adults about 1 5 per cent Duke Elder 1949) As to fundus pigmentation no figures are available for comparison

The values given do not represent average frequencies in congenital nystagmus because the present material has to some extent been selected as accounted for above In an unselected material the ophthalmological disorders would probably have been somewhat greater

Although Gamble s material (1934) has been less selected (exclusion of young children only) than the present one and a strict comparison is therefore

not possible the figures for visual acuity of the better eye and for squint are about the same in the two materials.

The refractive errors of other materials are not sufficiently specified to allow a comparison with the present one.

The ophthalmological disorders are certainly greater than in the general population. The number of cases with normal or almost normal ophthalmological findings is, however, sufficiently great to render improbable the theory that nystagmus is released from non-normal eyes.

B. Electronystagmographical examinations

I. The nystagmus type

The eye movements were pendular in a neutral zone (Fig. 1). They almost always increased at lateral gaze from this zone (Fig. 1) and then usually became jerky with the fast component in the direction of the gaze.

Out of the 90 cases 58 (65 per cent) had their neutral zone located in or close to the median plane of the head, 21 cases (23 per cent) to the right and 11 cases (12 per cent) to the left side of this plane. On fixation these 32 patients (35 per cent) with eccentric location of the neutral zone turned their heads in the direction opposite to the position of this zone and the eyes contrariwise, thus bringing the neutral zone in front of the body. The visual acuity increased by such a procedure, which was frequently noted by the author.

In connection with the symptom of turning the head it might be mentioned that shaking of the head was observed in 7 of the 90 cases (8 per cent).

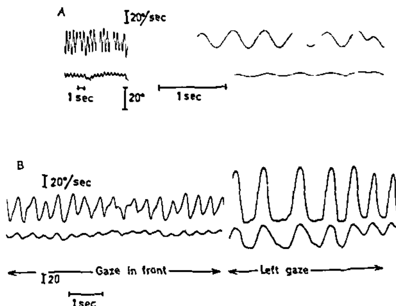


Fig. 1. A illustrates the jerky eye movements at gaze in front with the neutral zone. B shows how the pendular movements increase at gaze to the left. (A: case no. 40; B: case no. 37.) Upper curves: eye velocity. Lower curves: amplitude of nystagmus.

This symptom was most often evident only on excitation and was never pronounced

Comments Eccentric position of the neutral zone of nystagmus is relatively common The resulting compensatory head turning minimizes the nystagmus and increases the visual acuity

II Differences of nystagmus between light and darkness

In examining the differences of nystagmus between light and darkness in 89 cases the patients were instructed to look straight ahead all the time and to avoid fixing any near by object in light This instruction was given because in 15 cases tested the nystagmus always decreased when the patients fixed objects at distances of 40 30 and 20 centimetres from the eyes implying convergence

Closing the eyes in light does not only involve the exclusion of light but also a suppression of the eye movements (Fig 2) This was proved in the following way 85 patients were instructed to close their eyes in darkness The nystagmus thereby decreased in 82 cases and remained unchanged in 3

The results given below imply open eyes in darkness as well as in light

The nystagmus in darkness compared to light of 89 patients showed no decided or variable differences in 54 cases (61 per cent)

a decrease in 29 cases (32 per cent) and

an increase in 6 cases (7 per cent)

The changes were unmistakable in the two groups of decreasing and increasing (Fig 3) nystagmus in darkness

It is however necessary further to elucidate the variation in the group where no decided or variable differences of nystagmus were found when the

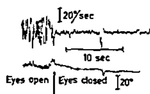


Fig 2 Decrease of congenital nystagmus by eye closure in darkness (Case no 27 Upper curve eye velocity Lower curve amplitude of nystagmus)

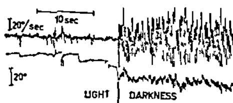


Fig 3 Increase of congenital nystagmus in darkness Eyes open (Case no 4 Upper curve eye velocity Lower curve amplitude of nystagmus)

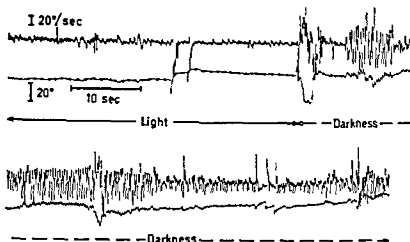


FIG. 4. Since the light has been turned off the congenital nystagmus increases after about 7 seconds and then shows sudden or gradual variations. (Case no. 5. The lower two records are continuations of the upper two. Upper curve, eye velocity. Lower curve, amplitude of nystagmus.)

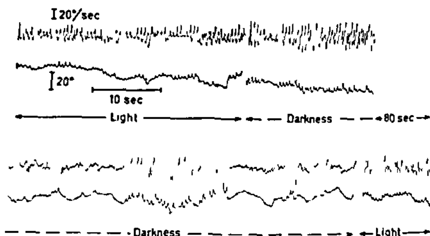


FIG. 5. Variations of congenital nystagmus in darkness. When the light is turned off there are at first no greater differences of nystagmus between light and darkness. Later when the room is lightened again the nystagmus is greater in light than in darkness. (Case no. 55. The lower two records are continuations of the upper two. Upper curve, eye velocity. Lower curve, amplitude of nystagmus.)

room was darkened. The variation of nystagmus in darkness in this group was usually obvious.

Frequently there were no immediate changes of nystagmus when darkening the room, these appearing gradually (Fig. 4).

The result of comparing nystagmus in light and darkness may be quite different on different occasions. Fig. 5 shows that there is no greater difference of nystagmus between light and darkness when the light is turned off. The nystagmus, however, shows an increase in light compared to darkness when the room is lightened again.

The depressing effect on nystagmus by eye closure in darkness is often not reversed by the opening of the eyes. Fig. 6 illustrates how the increase of

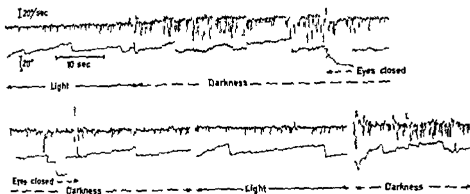


Fig 6 The congenital nystagmus increases when the light is turned off On eye-closure it then decreases and assumes about the same appearance as in light This appearance is kept also when the eyes are opened in darkness and when the light is turned on With repeated darkening of the room the nystagmus increases again (Case no 45 The lower two records are continuations of the upper two Upper curve eye velocity Lower curve amplitude of nystagmus)

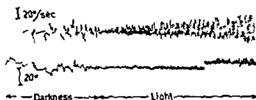


Fig illustrates the gradual increase of nystagmus when light has been turned on The difference between the irregular eye movements in darkness and the regular ones in light is also shown. (Case no 7 Upper curve eye velocity Lower curve amplitude of nystagmus)

nystagmus in darkness becomes depressed by eye-closure and how this depression remains also when the eyes are opened in darkness and the light is subsequently turned on

Gradual changes of nystagmus often seen in darkness may sometimes also appear when the light has just been turned on (Fig 7)

Comments The general opinion of congenital nystagmus as one which increases in light being a fixation nystagmus is based on the assumption that eye closure is equal to darkness in its effect

In this material where the differences of nystagmus between light and darkness were noted with the patients eyes open the *pattern of nystagmus in darkness* compared to light presented a great variability Apart from cases with decrease only and those with increase only *most of the cases exhibited no decided or variable differences*

The theory that the fixation is the trigger mechanism for congenital nystagmus has not been supported by this study

The variability of the nystagmus in darkness might be explained in the following way drowsiness is apt to occur in darkness The variations in the state of drowsiness occurring spontaneously produced by mental activity and ...ult are also reflected by *changes in the nystagmus*

pattern (cf. Mowrer, 1934; Wendt, 1951, Preber & Silfverskiöld, 1957, Mahoney, Harlan & Bickford, 1957; Lidvall, 1961, and Collins, Guedry, Posner & Knox, 1962)

Such an explanation makes it probable that the variations of nystagmus reflect the central background excitability No attention, however, was paid to the problem whether the changes in the nystagmus pattern coincided with sudden noises, speech of the examiner and so forth

III The influence of mephenesin on congenital nystagmus

Some preliminary testing of drugs as regards their influence on congenital nystagmus included barbiturates, promethazine hydrochloride, chlorpromazine hydrochloride, and mephenesin. From these studies mephenesin appeared to have the greatest depressing influence on congenital nystagmus and was therefore selected The composition of the mephenesin solution, the dose given and the way of administration, have been accounted for under the heading "Methods"

Mephenesin was given to 85 patients with congenital nystagmus

It could be shown that mephenesin caused

no changes of the nystagmus in 56 cases (66 per cent), and

a decrease of the nystagmus in 29 cases (34 per cent)

In the cases where mephenesin had effects the depression of nystagmus was usually moderate, but sometimes pronounced (7 cases) Fig 8 illustrates how the congenital nystagmus has become almost completely abolished by mephenesin

About 20 30 minutes after the administration of mephenesin the patients often became drowsy for a transient period of 15–20 minutes

In the cases where mephenesin caused a suppression of the nystagmus, the patients regularly stated spontaneously that their blurring of vision had decreased In these cases an increase of the visual acuity was generally found, usually about 0 1

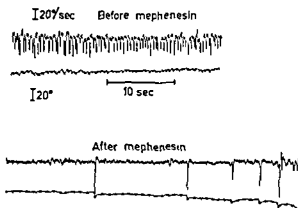


Fig 8 illustrates a pronounced effect of mephenesin on congenital nystagmus (Case no 7 Recordings in light Upper curve, eye velocity Lower curve, amplitude of nystagmus)

Of the 85 cases tested with mephenesin not one showed an increase of nystagmus at lateral gaze compared to the state before mephenesin had been given The tests for gaze nystagmus were performed by fixation 20 degrees to the right and to the left

Comments The depression of congenital nystagmus in ¼ of the cases is in accordance with the results of other authors (Bender & O Brien 1946 Bergman Nathanson & Bender 1951 1952) who also found that the effect of mephenesin was not regular

This failure to produce an increase of gaze nystagmus by mephenesin was presumably caused by testing the nystagmus during lateral gaze by fixation only 20 degrees to the right and to the left Blomberg (1957 1958) has used hexobarbitone B P (Evipan ®) and found that a deviation angle of 40 degrees was usually necessary to prove the existence of a gaze nystagmus It is probable that testing according to Blomberg would have revealed an increase of nystagmus at lateral gaze from mephenesin This has been found by many authors

II *The vestibular reactivity and the hearing acuity*

The vestibulo ocular responses were examined by caloric irrigations and rotations in the way accounted for under the heading Methods

The two methods showed no qualitative differences i e reactivity and non reactivity were always coincident as regards calorization and rotation

Eighty eight cases were examined calorically Of these the results were difficult to interpret in 9 cases (10 per cent)

Out of the rest 79 cases

49 (46 *per* cent) showed vestibulo ocular reflexes and 39 (44 per cent) did not

Fig 9 illustrates 2 cases A with and B without caloric reactivity

Eighty two cases were examined by rotation Of these the results were difficult to interpret in 9 cases (the same cases who showed identical difficulties on calorizations) and in 5 cases the records were technically insufficient These 14 cases were therefore omitted from analysis

Out of the rest 68 cases

37 showed vestibulo ocular reflexes and 31 did not

Fig 10 illustrates 2 cases A with and B without nystagmus reaction on rotation

In the evaluation of the cases with vestibulo ocular reflexes only the results from caloric irrigations were calculated This was done because (a) there were no discrepancies of the qualitative results from calorization and rotation (b) the stimulus on rotation was not constant from one case to another accounted for under the heading Methods and (c) the recording device of the angular velocity of the chair did not function properly during some periods

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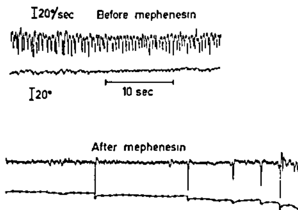


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Only the results from irrigations with water of 30°C in the right and left

Fig. 9. *A* shows normal and *B* failing nystagmus reaction from calorization (*A*, case no. 62, *B*, case no. 21. The lower two records of *A* and *B* are continuations of the upper two. Upper curve, eye velocity. Lower curve, amplitude of nystagmus.)

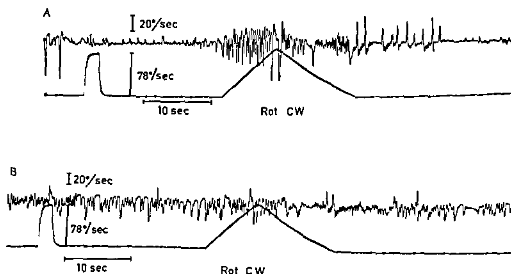


Fig. 10. *A* shows normal and *B* failing nystagmus reaction from rotation clockwise (*A*, case no. 22, *B*, case no. 23. Upper curves, eye velocity. Lower curves, angular velocity of the chair, the test representing 78°/sec. In *A* the acceleration is 11.8°/sec^2, in *B* 11.0°/sec^2. The angular velocity at the termination of the acceleration is 87.2°/sec in *A* and 89.0°/sec in *B*.)

TABLE 3 *Maximum eye velocity in cases of congenital nystagmus showing caloric reactivity*

Irrigations performed with water of 30°C right and left ear without drugs given and after mephenesin administration M = mean value, S = standard deviation n = number of observations

Case no	Max nystagmus in °/sec Without drugs 30°C Rt	Lt	After mephenesin 30°C Rt	Lt	Case no	Max nystagmus in °/sec Without drugs 30°C Rt	Lt	After mephenesin 30°C Rt	Lt
2	38	35	39	18	50	18	15		
4	36	31	16	16	54	12	10	12	16
9	15	15	12	15	55	34	40	34	31
13	27	27	25	23	57	17	18	17	18
16	40	43	36	40	58	40	40		
18	28	23	23	23	60	23	25	15	15
19	24	27	26	26	61	35	35	35	35
20	29	28	33	33	62	22	24	23	26
22	20	17	14	18	63	22	24	24	27
35	30	30	23	23	64	35	33		
36	21	21	22	20	66	16	15	11	11
	19	20	19	18	67	13	9		
38	44	40	32	32		7	4		
40	25	28	27	24	69	13	27	13	24
42	38	29	39	30	71	28	32	11	7
44	25	20	25	18	72	20	24	20	22
45	38	35	25	30	75	27	24	22	27
46	18	17			78	14	19	16	19
47	26	26	20	20	79	11	11		
48	27	20	18	16	80	28	28		
49	29	31	23	25	82	24	22	22	24
					n	42	42		
					M	25	25		
					S	9	9		
					n	84			
					M	25			
					S	9			
Calorizations without drugs and repeated after mephenesin					n	34	34	34	34
					M	26	26	23	23
					S	8	8	8	7
					n	68		68	
					M	26		23	
					S	8		7	

ear were counted since calorization in other ways (see under 'Methods') were relatively few

Out of the 40 cases with caloric reactivity, 33 were also tested under the influence of mephenesin Out of the 40 patients irrigated without any drugs

given, 2 were calorized on two occasions. Out of the 34 cases irrigated under the influence of mephenesin, 1 was calorized on two occasions.

Calorizations with water of 30°C in the right and left ear thus reached a number of 84 without and of 68 with mephenesin influence. The values of maximum eye velocity from these irrigations are given in table 3.

Two statistical analyses were made of the cases of congenital nystagmus showing vestibulo-ocular responses. One was concerned with a possible effect of mephenesin on the caloric reactivity, the other with a possible difference in caloric reactivity between this material and a normal material.

a) Effect of mephenesin on the caloric reactivity in cases of congenital nystagmus showing vestibulo-ocular responses.

The 68 calorizations made without drugs and repeated after mephenesin have been compared in the following way.

Two new series have been made, one of the differences in eye velocity before and after mephenesin from right calorizations, the other of the same differences from left calorizations. Each of these two series has been tested according to the null hypothesis of no difference, using the formula $t = M\sqrt{n}/S$ (t = significance level test). Figures from these calculations are shown in table 4.

TABLE 4. *Differences in eye velocity before and after mephenesin right ear and left ear*

A difference was stated to be + when the eye velocity was greater before than after mephenesin. M = mean value. S = standard deviation. t = significance level test. n = number of observations.

	Differences before and after mephenesin	
	Rt 30°C	Lt 30°C
n	34	34
M	+3 4	+3 1
S	5 [illegible]	[illegible] 3
t	3 4 ***	3 0[illegible] **

From this analysis it is evident that the caloric reactivity becomes significantly depressed by mephenesin in cases of congenital nystagmus.

b) Difference in caloric reactivity between a normal material and the cases of congenital nystagmus with vestibulo-ocular responses.

The 25 normal cases tested in the same laboratory and reported by Henriksson, Forssman & Dolowitz (1962) constitute the comparative material. The values of eye velocities from irrigations of the right and the left ear with water of 30°C without influence of drugs have been compared in the two materials.

The t test has been used for calculation of a possible difference between the two materials according to the formula

$$t = \frac{M_1 - M_2}{\sqrt{\frac{S_1^2(n_1-1)+S_2^2(n_2-1)}{n_1+n_2-2}}} \sqrt{\frac{n_1 \, n_2}{n_1+n_2}}$$

The test showed no significant difference between the two materials, t being 1.129 (not sign.).

Audiometric examinations were performed because of the high frequency of abolished vestibulo-ocular reactivity. It was reasonable to assume that if this abolished reactivity was due to a peripheral vestibular block there would also probably be defects in the hearing function because of the close anatomical connections between the two parts of the eighth nerve.

The audiometric examinations were performed by well trained technicians at the audiologic laboratory of the ENT Department in Lund.

Out of the 90 cases of congenital nystagmus, 85 were examined with pure tone audiometry, 2 of them also with speech audiometry. The results were normal with the following few and mostly insignificant exceptions.

Seven cases showed inner ear hearing loss, probably induced by noise. Three cases exhibited conduction hearing loss. One case showed a confusing hearing loss, probably of the perceptive type.

Comments. It is known from a few reports in the literature that the vestibulo-ocular reactivity may be absent in some cases of congenital nystagmus. The systematic study of this reactivity in the present great material has shown a surprisingly high frequency of abolished vestibulo-ocular reflexes with no significant changes in hearing acuity.

DISCUSSION

The ophthalmological disorders in the cases of congenital nystagmus reported in this study are probably smaller than those of an unselected material of the same disease. From the frequency figures of visual acuity, refractive errors and squint in 86 cases of the disease it is apparent that eye symptoms are common and not infrequently dominate the clinical picture. The number of cases with normal or almost normal vision and with absent or small refractive errors (37 resp. 30 per cent in the better eye) is sufficiently great to warrant the conclusion that the ophthalmological disorders cannot reasonably be the *cause* or the trigger mechanism of the nystagmus. Such a conclusion might, however, be invalidated by the following three hypothetical possibilities.

(1) Functional disturbances may exist.

(2) Cases with decreased vision but with insignificant refractive errors could be explained on the assumption that gross refractive errors had been present during the first four months of life when the macula is dependent on sharp images for developing properly.

(3) There is not one single cause of congenital nystagmus but more than one. The more pronounced ophthalmological disorders would then be the

cause or the trigger mechanism of the nystagmus if they had existed from birth. There would be a different cause in cases of insignificant eye symptoms.

The principal objection to the idea that congenital nystagmus is due to defects of the eyes, however, is this: it has often been observed (and reported in the literature) that nystagmus is present the first day of life when fixation is impossible irrespectively of the state of the eyes. In four cases of the present material such an occurrence is highly probable. Because of the inheritance of the disease in the resp. families the mothers of these patients paid particular attention to the eyes of their children.

It is not known whether the defects of the eyes are directly due to the unknown factor in the disease or indirectly to the nystagmus. That the eye movements give rise to some depression of the visual acuity is apparent from the findings that this ability increases when the nystagmus is minimized by mephenesin or by the eyes being brought into the neutral zone. According to Franceschetti, Monnier & Dieterle (1952) non-coinciding neutral zones for the two eyes are frequently the cause of squint.

The differences between light and darkness in nystagmus consist of a depression of the nystagmus at eye closure according to the general opinion. This has been fully confirmed in the present study.

When the differences are evaluated from a state of open eyes in darkness as well as in light the result, however, is quite different. In that case only 1/3 of the cases exhibit a decrease of nystagmus in darkness compared to light while 7 per cent show an increase and the greater part (60 per cent) is unchanged in this respect.

The records of these undecided cases usually show variations in the intensity and the rhythm of the nystagmus in darkness. It does not seem improbable that these variations, at least in some of the cases, reflect changes in the degree of wakefulness. The types of the variations indicate central influences.

In this study it has been shown that changes in light and darkness influence the nystagmus pattern in different ways and that the designation of congenital nystagmus as a *fixation nystagmus is relevant only in 1/3 of the cases.*

The influence of mephenesin on congenital nystagmus consisted of a depression of the spontaneous nystagmus with a simultaneous increase of the visual acuity in 1/3 of the cases and also of a significant decrease of the calorically induced nystagmus in cases of preserved vestibular reactivity irrespectively *of the effect of the drug on the spontaneous nystagmus.*

Mephenesin has a predominant effect on multisynaptic pathways and depresses the facilitatory part of the brain stem reticular formation to the same extent as or more than the inhibitory part (Kaada 1950). The frequent but not always ascertainable effects of the drug on congenital nystagmus can be explained by this mode of action and may illustrate the dependence of congenital nystagmus on the degree of central inhibition.

The vestibular reactivity in congenital nystagmus was absent in 44 per cent

as evaluated from the vestibulo ocular responses. As the hearing acuity was essentially normal and episodes of dizziness neglected it was assumed that the cause is most probably of a central and not of a peripheral nature.

Such an assumption is supported by the results of animal experiments of Szentagothai & Schab (1956). They showed that vestibulo ocular reflexes could be abolished by stimulation of a midbrain area corresponding to the nucleus of Darkschewitsch.

In order further to investigate the problem of labyrinthine reactivity in the absence of vestibulo ocular reflexes supplementary studies have been made by recording the vestibulo spinal reactions. The results of these examinations are reported by the author in another place of this journal.

ZUSAMMENFASSUNG

Es wurden 90 Fälle mit kongenitalem idiopathischen Nystagmus von Ophthalmologen und vom Autor hauptsächlich elektrookulographisch untersucht und folgende Befunde erhoben.

In über einem Drittel der Fälle war die Sehschärfe des besseren Auges fast oder völlig normal. Refraktionsfehler fanden sich nur bei der Hälfte des ganzen Materials. Strabismus wurde in 16 % festgestellt.

Die neutrale Zone für die normalen Pendelbewegungen des Auges war in 35 % der Fälle so exzentrisch gelegen, dass die Fixation eine Wendung des Kopfes auslöste.

Der Nystagmus zeigte bei Untersuchung in Dunkelheit gegenüber den Verhältnissen im Hellen in fast allen Fällen bei geschlossenen Augen eine Abnahme, bei geöffneten Augen dagegen unterschiedliche Grade (in 33 % Abnahme, in 7 % Zunahme und in 60 % unverändertes oder variierendes Ausmass).

Mephenesin verminderte in einem Drittel der Fälle den spontanen Nystagmus und verursachte eine signifikante Abnahme von kalorisch ausgelöstem Nystagmus.

Die vestibulo okulare Reaktion war bei 10 % der Fälle unklar, bei 46 % normal und fehlte völlig bei 44 %. Das Audiogramm war bei allen Fällen annähernd normal.

Es wird angenommen, dass die vestibulo okulare Areflexie durch zentrale Einflüsse bedingt wird.

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University of Lund Sweden

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JUGULAR SYNDROME

With special reference to the diagnostic value of retrograde jugularography

TOMAS GEJROT
Stockholm, Sweden

From the Department of Otolaryngology (Head Prof C-A Hamberger), Karolinska Sjukhuset, Stockholm

Three cases of tumours involving the jugular foramen are reported, in one the growth was intracranial, in one extracranial and in the third it originated from the superior bulb of the internal jugular vein The anatomy of the jugular foramen and the clinical symptoms consequent on the involvement of the IX, X and XI cranial nerves are described Problems of diagnosis are discussed and the value of retrograde jugularography is stressed

The term jugular syndrome, otherwise known as Vernet's syndrome, denotes the group of symptoms arising from paralysis of all the cranial nerves that pass through the jugular foramen The tumours or other growths that exert pressure on the nerves and thus cause the paralysis may be intra or extracranial or situated in the foramen itself With a growing interest among neck surgeons in operative treatment for tumours around the base of the skull, new methods for diagnosing these conditions have been introduced On the assumption that pressure on the nerves within the jugular foramen will also affect the internal jugular vein, which is situated just behind the nerves, a special form of phlebography of the internal jugular vein, retrograde jugularography, has been developed and tested at the Karolinska Hospital as a diagnostic aid in cases of this syndrome In this article three typical cases are reported in which the method has been used

Anatomy

The jugular foramen is formed by the jugular notch on the occipital bone, and the adjacent temporal bone The lateral and medial parts are separated by the intrajugular process The posterior component transmits the initial part of the internal jugular vein and is on an average 12 × 8 mm in size (Rudinger, 1876) The medial anterior part, which is known as the pars nervosa, transmits the IX, X and XI cerebral nerves and the inferior petrosal sinus (Fig 1) It is on an average 3 × 5 to 4 × 6 mm The right jugular foramen is usually larger than the left, Linser (1900) found that the right foramen was the larger in 662 cases out of 1022, while in 246 the left was the larger, in only 114 cases were they the same size There would seem to be no rela-

tionship between the size of the jugular foramen and other foramina in the base of the skull (Lindblom, 1936)

The internal jugular vein begins as a funnel shaped dilatation, the superior bulb in the posterior compartment of the jugular foramen, and continues down behind the carotid artery The transverse sinus and the vena canaliculi cochlea emerge into the superior bulb of the jugular vein The inferior petrosal sinus may also reach the jugular vein in the jugular foramen

The glossopharyngeal nerve passes through the anterior compartment of the jugular foramen, lateral and anterior to the vagus and accessory nerves, from which it is separated by a fibrous septum

The nerve then passes down between the internal jugular vein and the internal carotid artery The glossopharyngeal nerve gives off the tympanic nerve, which distributes sensory fibres to the mucous membrane lining the tympanic cavity and auditory tube, and the parasympathetic secretomotor fibres to the parotid gland

The vagus nerve is situated just behind the glossopharyngeal nerve and passes through the jugular foramen accompanied by the accessory nerve It follows the common carotid artery and the internal jugular vein, where it lies in the groove between the two vessels

The accessory nerve is a motoric nerve which innervates the sternocleido mastoid and the trapezius muscles The accessory trunk passes with the vagus nerve through the jugular foramen and then divides into the internal and external rami The former contains the cranial root of the nerve and joins the vagus nerve below the superior ganglion The external ramus constitutes the spinal root of the nerve and descends laterally and backwards crossing the internal jugular vein, piercing the deep surface of the sternocleidomastoid muscle and continuing to the trapezius

The hypoglossal nerve is often damaged with the aforementioned cranial nerves It is transmitted by the hypoglossal canal and its initial stretch is situated medially and posterior to the vagus nerve

Clinical Features

It is rare for only one of the nerves passing through the jugular foramen to be damaged A number of syndromes have been described in which different groups of the last four cranial nerves are involved

The symptoms resulting from damage to the glossopharyngeal nerve include impairment of the sensibility of the posterior third of the tongue the tonsils and the pharynx and of the sense of taste in the affected part of the tongue The salivary secretion is also affected The condition is diagnosed by tests of the taste and pharyngeal reflex

Isolated damage to the vagus nerve in the posterior cranial fossa is rare, the aforementioned nerves usually also being involved The cause generally lies with a tumour, in most cases a glomus tumour (Brain 1960) The signs consist of unilateral paralysis of the palate and pharynx, which though not necessarily giving rise to subjective symptoms are manifested in the intona

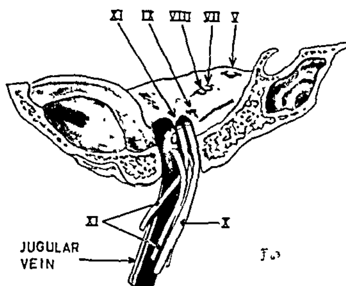


Fig. 1. The jugular foramen with pars vascularis (internal jugular vein) and pars nervosa (IX–XI cranial nerves)

tion and in tests of the pharyngeal reflex. The chief sign is paralysis of the recurrent laryngeal nerve. Autonomous symptoms in cases of unilateral damage to the vagus nerve are usually of a minor nature

Involvement of the accessory nerve results in paralysis of the sternocleidomastoid and trapezius muscles The outline of the former muscle on the neck is abnormal, the shoulder drops and the border of the trapezius muscle is not so easily recognizable by palpation as usual The power of the shoulder and arm is reduced

Report of Cases

Case 1

A woman aged 51 years, who had been suffering from pain and stiffness of the neck for one year (since 1961) A month or so after the onset of these symptoms she noticed that the left shoulder had dropped At the same time there was swelling in the region of the left parotid gland, accompanied by high temperature For one week there was swelling on the right side also and parotitis was therefore suspected At the beginning of August 1961, there were hoarseness, difficulty in swallowing, secretory stasis and atrophy of the left side of the tongue On admission to hospital, September 1961, there was a firm infiltration behind the left angle of the jaw At a neurologic examination the left shoulder was found to have dropped, and it was difficult to recognize the sternocleidomastoid muscle and the upper part of the trapezius muscle by palpation on the left side There was considerable atrophy of the tongue, with a leftward deviation, and paralysis of the palate, throat and larynx, the left vocal fold was stationary Tomography disclosed destruction of the occipital condyle but not of the jugular foramen Biopsy specimens from the infiltration showed vegetations of a sympathoblastoma



Fig. 4. Retrograde jugularography. Antero-posterior view. Normal findings.

Case 9

A woman of 54 years with hoarseness as the first symptom 4 years previously (in 1957). Examination at the local hospital showed paralysis of the left recurrent laryngeal nerve and evidence of the *signe rideau* phenomenon. The patient was referred to the Department of Neurology where pneumoencephalography and angiography of the vertebral artery gave no significant findings. Later on there was fatigue and in April 1961 the patient noticed an impairment of the hearing and pulsating tinnitus in the left ear. Puncture of the inflamed and bulging tympanic membrane produced severe bleeding. Radiographs of the jugular foramen brought to slight destruction of the left side and the presence of a glomus tumour was suspected. On admission to the

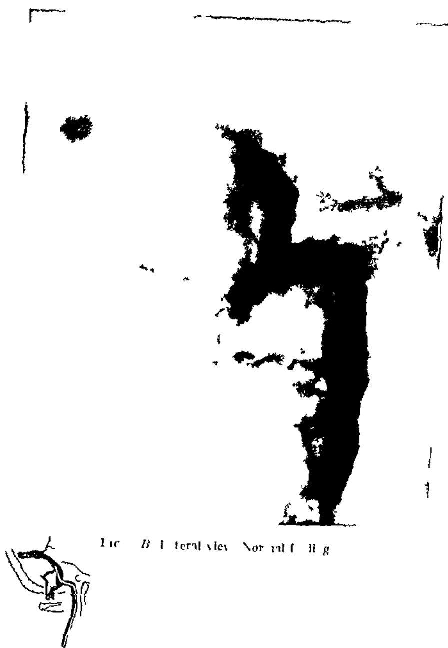


Fig. B. Lateral view. Normal f... g

Karolinska Hospital in November 1961 there was left sided hearing loss, inflammation and thickening of the tympanic membrane, atrophy of the left of the tongue, the *signe rideau* phenomenon, paralysis of the left recurrent laryngeal nerve, slight facial paralysis on the left side and atrophy of the left sternocleidomastoid and trapezius muscles. Tomography confirmed destruction of the left jugular foramen. At operation the jugular vein was exposed from the neck and from the mastoid process after ligating the external carotid artery. On opening the vein from both directions a thrombus-like tumour ... cm long and with the consistency of rubber was removed. There was no tumour tissue in the sigmoid sinus. Histologic examination confirmed the diagnosis of glomus tumour. The recovery was uneventful and the tinnitus and dullness disappeared. Post operative X ray therapy was carried out.



Fig. 3. Case 1. Left: the internal jugular vein is dislocated laterally (arrow at catheter). The common facial vein is greatly enlarged. The tumour is surrounded by visualized veins.

Case 3

A woman of 23 years who had been hoarse for one year (since 1961). In the spring of 1962 paralysis of the left recurrent laryngeal nerve was discovered. Since there was also paralysis of the palate and deviation of the tongue the patient was referred to the Department of Neurology at the Serafimer Hospital. A fully developed jugular foramen syndrome was found with paralysis of the IX–XII cranial nerves. Audiograms were normal but there was a spontaneous leftward nystagmus of the third degree. Radiographs of the cranium showed a greatly widened left jugular foramen but no destruction. Encephalography disclosed an extra cerebral expansive process on the left side in the posterior cranial fossa near the foramen magnum. At transcranial operation a walnut sized tumour was removed which was firmly attached to the IX cranial nerve and which occupied the whole jugular foramen (Fig. 5). Histologic examination showed this to be a neurofibroma. Post operative

In the cases of the jugular syndrome the clinical picture can provide a fairly accurate impression of the position and extent of the tumour. For intracranial tumours in this region there are well developed radiographic techniques such as angiography and encephalography. For extracranial tumours in the region of the jugular foramen, tomography of the cranial base is the most important method of examination. In cases 1 and 2 tomography revealed destruction of the occipital condyle and of the jugular foramen, respectively. A widening of the foramen such as that seen in case 3 need not be pathologic (Linser, 1900).

A tumour in the foramen region must probably occlude the vein before it can destroy the bone or damage the nerve. Retrograde jugularography in cases of glomus tumours, for instance, demonstrated that there was clamping of the vein before the neurologic symptoms developed.

The base of the skull constitutes a frontier for the neurosurgeon and ear surgeon. Some regions in the base are still regarded as a sort of no man's land and the jugular foramen is one of them. A tumour that grows through the foramen may call for both intra- and extracranial approaches. Jugularography may then provide a valuable link between the two fields for surgery. Case 3 provides an excellent example of this. In case 2 jugularography was important in showing the position and extent of the tumour and deciding the surgical approach of choice.

ZUSAMMENFASSUNG

Drei Patienten mit Tumoren in dem Foramen jugulare sind beschrieben. Die Tumoren waren teils in dem Bulbus und teils extra- und intrakraniell gelegen. Anatomie und diagnostische Probleme sind diskutiert und der Wert von retrograder Jugularographie ist betont.

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Department of Otolaryngology
Karolinska Hospital, Stockholm 60
Sweden

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HABITUATION EFFERENCE AND VESTIBULAR INTERPLAY

IV Rotatory habituation of the vertical semicircular canals

E Fluur and L Mendel
Stockholm, Sweden

From the Department of Otolaryngology (Head Prof C A Hamberger, M D) Karolinska Sjukhuset, Stockholm 60

Twenty two persons were subjected to rotary habituation of the vertical semicircular canals The posterior canals were habituated in 12 subjects and the anterior canals in 10 Initially tests were made of the post rotatory nystagmus duration in both directions Thereafter the patients were rotated in the same direction 12 16 times Finally a fresh post rotatory test was made and the values were compared with the initial values

After the habituation of the posterior canals there was obtained in two subjects a directional preponderance downwards while nine subjects had reduced reactions in both nystagmus directions One subject had primarily a nystagmus upwards which increased somewhat in intensity after habituation

Habituation of the anterior vertical semicircular canal gave eight cases which had directional preponderance upwards two even spontaneous nystagmus upwards while two persons had reduced reactions in both nystagmus directions All of the eight subjects who did not get spontaneous nystagmus had instead a secondary nystagmus upwards

The results show that the vertical canals react differently from the horizontal canals and that they also react differently among themselves upon habituation Various explanations of this are discussed

The vertical semicircular canals differ in several respects from the horizontal canals Anatomically they are twice as numerous as the horizontal ones and moreover they are spatially located in such a way that several possibilities of physiological combination can exist Functionally speaking they also react in the opposite way to the horizontal canals inasmuch as their electrical activity increases upon an ampullofugal endolymph current and diminishes upon an ampullopetal one (Lowenstein & Sand 1940) Anatomical studies have shown that through a three neuron pathway they are all in connection with a straight eye muscle in one eye and with an oblique muscle in the other (Szentagothai 1950) Stimulation of the two anterior vertical semicircular canals gives an elevation of both eyes (Fluur 1959) and a nystagmus downwards whereas instead a stimulation of the posterior vertical canals gives a depression with a nystagmus upwards Upon rotatory stimulation clockwise in a bitemporal axis with the back in the direction of movement a postrotatory nystagmus upwards is obtained when the chair is suddenly

stopped. The same stimulation in the contrary direction gives a nystagmus downwards instead. It is well known that this postrotatory vertical nystagmus has a considerably shorter duration than the corresponding horizontal nystagmus.

The above-mentioned anatomical and physiological differences between the horizontal and the vertical semicircular canals have prompted the question whether the vertical canals can be habituated as easily as the horizontal ones and in that case how this habituation occurs.

MATERIALS AND METHODS

For the investigation 22 vestibularly normal subjects were used. In a specially constructed rotation chair (Stille-Werner, modification Fluur) adaptable for centric or eccentric stimulation, the subjects were placed lying down on their left side with the axis of rotation passing through both the external auditory canals. Initially a postrotatory test of upward and downward nystagmus was made. The subject was accelerated at 1°/sec² up to a speed of 90°/sec, after which constant speed was maintained for 2 min. The chair was then stopped immediately and the duration of the postrotatory nystagmus was recorded electronystagmographically with the subject's eyes open in complete darkness (Fluur & Mendel 1963).

The subjects were then divided into two groups. In one group, comprising 12 persons, the posterior vertical semicircular canals were habituated and in the other, consisting of 10 persons, the anterior canals were habituated. The procedure of habituation was that each subject was accelerated at 1°/sec² up to 90°, after which the chair was stopped immediately. This was repeated in the same direction 10–16 times. After habituation a final testing of the function of the two vertical semicircular canals was made by investigation of the postrotatory nystagmus upwards and downwards. The results were compared with those obtained before the habituation.

The recording was carried out electronystagmographically by electrodes placed above and below one eye in the plane of the pupil when the subject was looking straight ahead. A pair of rubber goggles which excluded all incoming light was placed before the eyes, which were kept open during the whole investigation. During the acceleration the subject was spoken to and asked to look calmly ahead without fixing his gaze. This was done partly to avoid disturbing voluntary eye movements when the recording of the postrotatory nystagmus was about to begin and partly to prevent a decline in the waking state of the subject. Otherwise the monotony of the investigation and the subject's comfortable position might have led to his falling asleep.

RESULTS

It was already apparent at the outset that in this investigation the task of evaluating the curves was more difficult than had been the case with the horizontal habituation. The fact that the vertical nystagmus was of consider-

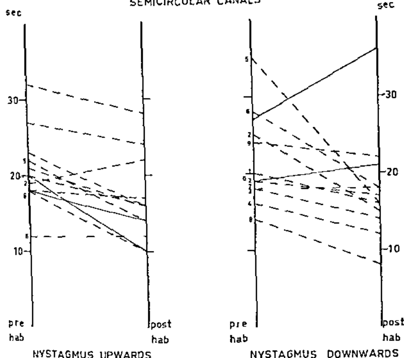


Fig 1 Rotatory habituation of the posterior semicircular canals Group 1 (continuous line) Nystagmus upwards decreases but nystagmus downwards increases Group 2 (broken line) Reduction both for upward and downward nystagmus

ably shorter duration than the horizontal nystagmus meant that the differences between the nystagmus durations before and after habituation also became less With the recording method which was used with two derived and rectified channels and six traditional nystagmography channels with different amplification this did not however offer any difficulties in determining the duration of the nystagmus in the different cases

The habituation of the posterior vertical semicircular canals gave the following results (Fig 1) After the habituation two persons had a diminished postrotatory nystagmus upwards but instead an increasd nystagmus downwards (Group 1) Nine patients had a reduction of the nystagmus duration both for upward and for downward nystagmus (Group 2) One subject had already before the habituation a spontaneous nystagmus upwards in spite of the fact that his eyes were kept open After habituation this nystagmus had if anything increased upwards but instead had decreased slightly downwards

Before the habituation four persons had after a stimulation which post rotatorily had given nystagmus downwards a secondary nystagmus upwards These were cases which at the postrotatory test had all shown a directional preponderance for upward nystagmus In three of these cases the secondary nystagmus disappeared after the habituation

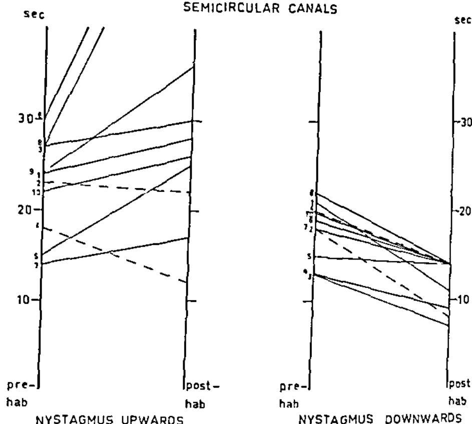


Fig. 2. Rotatory habituation of the anterior semicircular canals. Group 1 (continuous line): Nystagmus upwards increases but nystagmus downwards decreases. Group 2 (broken line): Reduction both for upward and downward nystagmus.

Three subjects had before the habituation a directional preponderance downwards and also obtained a secondary nystagmus downwards after an earlier postrotatory nystagmus upwards. After the habituation all three cases still showed a secondary nystagmus downwards which in general had increased in intensity.

The persons whose anterior vertical semicircular canals had been habituated showed the following reactions (Fig. 2). Eight subjects had longer nystagmus durations upwards, two of them indeed even had a spontaneous nystagmus upwards. The reaction times for downward nystagmus showed reduced durations in these cases (Group 1). Two persons had shorter nystagmus durations for both upward and downward nystagmus (Group 2).

All of the eight persons belonging to both Group 1 and Group 2 who after habituation of the anterior vertical semicircular canals did not get spontaneous nystagmus upwards, instead obtained a secondary nystagmus upwards after stimulations which had first produced downward postrotatory nystagmus. A comparison between the nystagmus upwards and downwards showed a preponderance for upward nystagmus both before and after the habituation.

There was no dysrhythmia after habituation either of the anterior or of the

posterior vertical semicircular canals Nor were there found any prolongations of the latency times such as had been found upon caloric habituation (Fluur & Mendel 1962)

DISCUSSION

It proved more difficult to habituate the vertical semicircular canals than the horizontal canals The two types of canal also react differently to a rotatory habituation The explanation probably is that the vertical semicircular canals have a considerably higher stimulation threshold than the horizontal canals (evidence for this will be presented in a later work) The same rotatory stimulus then gives fewer impulses from the vertical semicircular canals up to the centres which govern the efferent activity and therewith the habituation

The results of the investigations argue in favour of the hypothesis that the vertical semicircular canals not only differ from the horizontal canals in their mode of reaction but also react differently among themselves The habituation of the anterior canals gave mainly results according to Group 1 whereas the posterior canals above all reacted in accordance with Group 2 This suggests that it is much easier to hyperpolarize the anterior canals with the aid of the efferents than to hyperpolarize the posterior canals Two subjects had such an increase of the depolarization pressure in the posterior canals that spontaneous nystagmus upwards appeared whereas the remaining subjects had a secondary nystagmus upwards after each stimulus which had given a primary nystagmus downwards The reason why the two cases belonging to Group 2 also had secondary nystagmus upwards was that as Fig 2 shows the duration for upward nystagmus is longer than for downward nystagmus although both are reduced This may be interpreted by the hyperpolarization having proceeded further in the anterior vertical canals than in the posterior ones

The above mentioned conclusion was also supported by the results from the group whose anterior canals had been habituated Here there were nine cases where both canals were hyperpolarized and gave reduced reactions whereas only two cases gave hyperpolarization only from the posterior canals Both had initially a directional preponderance downwards and one even had secondary nystagmus downwards after earlier upward primary nystagmus As an expression of the fact that the difference in activity between the two canals *increased after* habituation there was also found an increasing secondary nystagmus

There may be several explanations for the fact that different results were obtained upon the habituation of the anterior and the posterior canals As a result of the *anatomical localization* of the canals in relation to the sagittal line there may be upon rotation a stronger stimulation of the posterior canals which would lead to a stronger input and greater stimulation of the centres which release the efferent activity Another possibility is that even with the subject s eyes open there is a certain predominance in the tone of either the elevators or the [illegible] essors which would lead to the *stimulation* of the posterior

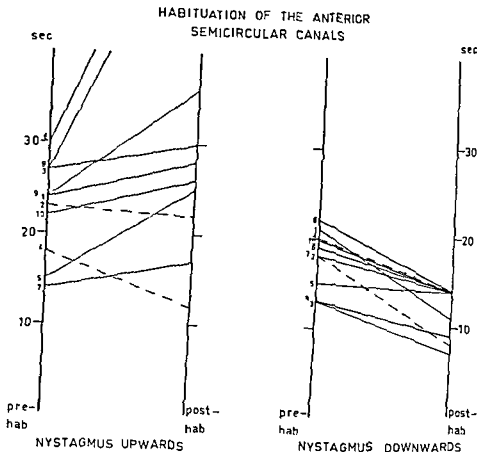


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canals giving a stronger stimulation to the eye muscles than would be given by the same stimulus from the anterior canals. A third possibility is differences in the relation between afferents and efferents in the two canal systems. Which of these three explanations is the most likely cannot be determined with the present study but will require further investigations, both anatomical and physiological.

ZUSAMMENFASSUNG

An 22 Personen wurde eine rotatorische Gewöhnung der vertikalen Bogengänge gemacht. In 12 Fällen wurden die hinteren Bogengänge angewöhnt und in 10 Fällen die vorderen. Zuerst wurde die postrotatorische Nystagmusdauer in beiden Richtungen geprüft. Danach wurden die Patienten in derselben Richtung 12–16mal rotiert. Zuletzt machte man einen neuen postrotatorischen Test, dessen Werte mit den anfänglichen verglichen wurden.

Nach der Gewöhnung der hinteren vertikalen Bogengänge bekamen zwei Personen eine Nystagmusbereitschaft nach unten, während man in neun Fällen gesenkte Reaktionen in beiden Nystagmusrichtungen fand. Eine Person hatte primär einen Nystagmus nach oben, der nach der Gewöhnung etwas intensiver wurde.

Die Gewöhnung der vorderen vertikalen Bogengänge gab in acht Fällen eine Nystagmusbereitschaft nach oben — zwei Personen bekamen sogar einen Spontannystagmus nach oben — und in zwei Fällen gesenkte Reaktionen in beiden Nystagmusrichtungen. Die acht, die keinen Spontannystagmus erhielten, bekamen statt dessen einen Sekundärnystagmus nach oben.

Die Ergebnisse zeigen, dass die vertikalen Bogengänge anders als die horizontalen reagieren und auch, dass sie nach einer Gewöhnung untereinander verschiedentlich reagieren. Verschiedene Erklärungen dafür werden diskutiert.

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Department of Otolaryngology, Karolinska Sjukhuset, Stockholm 60, Sweden

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PARATYPHÖSE SINUITIS MAXILLARIS

Erich Hartmann
Sonderborg, Danemark

Aus der Infektionsklinik des Kreiskrankenhauses Arvika, Schweden (Chef U Murray Hals-Nasen Ohrenarzt G Wessling)

Es wird von einer eitrigen Kieferhohlenentzundung berichtet, deren Ursache eine Salmonelleninfektion ist (S typhi murium) Nach erfolgter Kieferhohlenresektion ist diese keimfrei Es werden darauf kurz die Komplikationen der Salmonellenerkrankungen im Hals Nasen–Ohrengebiet geschildert

Die Sinuitis gehort zu den taglichen Angelegenheiten des Facharztes, jedoch sei der folgende Fall dem Leser nicht vorenthalten Zunachst die Krankengeschichte

Ein 70jahriger Patient erkrankt ungefahr 14 Tage vor der Einlieferung an heftigen Diarrhoen und Erbrechungen Die bakteriologische Untersuchung ergibt eine Salmonellainfektion, worauf die Einlieferung erfolgt Die gastro intestinalen Beschwerden klingen schnell ab Der Patient klagt anfangs über leichten Schnupfen, der, nach vorubergehender Besserung, in eine eitrige Sekretion der rechten Nasenhalfte ubergeht Die Hals Nasen Ohrenuntersuchung ergibt Eiter der rechten cav nasi, darüber hinaus normaler Befund

Bei der Punktion der rechten Kieferhohle entleert sich dicker, stinkender Eiter Die bakteriologische Untersuchung zeigt folgendes Kulturen der Salmonella typhi murium (Breslau) Ausserdem in geringen Mengen Staphylococcus aureus

Da nach mehreren Punktionen keine Besserung eintritt, entschliesst man sich zur Kieferhohlenresektion a m Caldwell Luc Der Eingriff wird durch eine heftige Blutung erschwert, erst nach der Unterbindung der a carotis ext kann die Operation beendet werden Die Schleimhaut der Hohle ist leicht polypos, es gibt makroskopisch keine Anzeichen einer Ostitis Histologischer Befund Chronische Entzundung ohne Anzeichen einer Malignitat Postoperativer Verlauf normal Spatere bakteriologische Untersuchungen des Spuhlwassers der Kieferhohle zeigen kein Wachstum der Salmonellen Leider war der Patient bei der Entlassung noch Bazillenausscheider trotz intensiver Behandlung mit verschiedenen Antibiotica

DISKUSSION

Klinisch sind typhose und paratyphöse Erkrankungen kaum voneinander zu unterscheiden, und die gleichen Komplikationen treten im Hals-Nasen Ohrengebiet auf Daher stützen sich meine Angaben zum Teil auf Literatur uber den Typhus

Wie allgemein bekannt sein durfte, erfolgt oft eine Verschleppung der Keime haematogen Diese werden dann in verschiedene Organe ausgestreut Es sei jedoch gleich hervorgehoben, dass diese Komplikationen seltener geworden sind nach Einführung der antibiotischen Behandlung (Bollobás, 1959)

Wenden wir uns dem Kehlkopf zu, so findet man hier Perichondritiden und Geschwursbildungen (Bingold, 1959, Hajek, 1932) Man sprach fruher von einem Laryngotyphus (Rokitantsky cit Bingold, 1952)

Mit zum Anfangsbild mancher dieser Erkrankungen gehoren die Angina, und man hat im Belag Salmonellen gefunden

In einem Typhus-Krankengut aus den Jahren 1937–1947 kamen Ohrkomplikationen zu 1,25 % vor Diese Falle gehen gern mit Nasen-Rachenkatarrhen einher Bei ungefahr ¼ dieser Falle wurde die Mastoidectomi durchgefuhrt (Bollobás, 1959) Weiter wird von Labyrinthiden berichtet (Robin, 1959)

Nühsmann (1926) erwahnt die typhose Sinuitis als haufige Komplikation Sie wird jedoch oft von den Allgemeinerscheinungen uberdeckt Moglicherweise besteht oft eine Ostitis als Primarerscheinung Salinger (1960) erwahnt in seiner Übersicht der Sinuserkrankungen nicht die Salmonellen

Eine Mischinfektion lasst sich natürlich, nicht ganz von der Hand weisen, jedoch erfolgt nach Bingold (1952) eine Eiterung haufiger bei den paratyphosen Erkrankungen Dies andert auch nichts an der Tatsache, dass der Patient Paratyphusbazillen via Nase ausschied, und erst der Eingriff diesen Einhalt gebot

SUMMARY

A case of sinusitis maxillaris caused by salmonella typhi murium Treatment by Caldwell-Luc operation After this no bacilli can be demonstrated Typhoid and paratyphoid diseases of the ear, nose and throat are shortly mentioned

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Orstedsgade 81 Sonderborg Denmark

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OSTEOID OSTEOMA IN THE MANDIBULAR CONDYLE

Case report and survey of the literature

PER OVE LIND and KURT HILLERSTRÖM
Stockholm Sweden

From the Department of Dental Histopathology (Head G Bergman) and the Department of Prosthetics (Head Björn Hedegård) Royal School of Dentistry Stockholm

A case is described of an osteoid osteoma in the mandibular condyle a location not earlier reported A 48 year old man had an ankylotic mandibular joint accompanied by arthralgia, symptoms which returned despite treatment The condyle was therefore amputated and an osteoid osteoma was found in it No changes were noticeable in the X ray

The literature on osteoid osteomata, especially with reference to their genesis is discussed The pathogenesis of the ankylosis is considered against the background of earlier treatment and the operative method is described In conjunction with the histopathological description the possible causes of the cartilaginous lesions in the condyle their possible relation to the osteoid osteoma and the differential diagnosis of the osteoid osteoma are discussed

INTRODUCTION

The concept of osteoid osteoma was introduced by Jaffe in 1935 and is now generally accepted as a clinico pathological entity

The osteoid osteoma is characterized clinically as a small but painful bone lesion It is most common in young persons and more usual in men than in women It is generally located in the tibia or femur (50 per cent) but all bones may be attacked Only one case however has earlier been reported in the mandible in the body immediately anterior to the angle by Foss Dockerty & Good (1955) No case of osteoid osteoma in the mandibular condyle has been reported earlier The total number of cases of osteoid osteoma in the world literature was calculated by Pines Lavine & Grayzel in 19[illegible] to have been about 150

Terminology and Definition

Prior to Jaffe s definition of osteoid osteoma the lesion was generally regarded as a type of chronic bone abscess and was described under a number of confusing designations as Garre s sclerosing non suppurative osteomyelitis osteomyelitis with annular sequestrum etc and was often confused with Brodie s abscess What is now meant by osteoid osteoma is a very painful but small bone lesion its maximum diameter seldom exceeding 2 cm and consisting of a central nidus of osteoid and atypical bone with a perifocal reactive zone in the surrounding bone

Clinical Picture

1. Pain is the most characteristic clinical symptom. Occasional and mild at first, it becomes increasingly severe and more persistent as the osteoid osteoma grows. Pain may occur long before any lesion is observable radiographically.
2. Point tenderness over the lesion.
3. Slight local swelling.
4. Stiffness of a joint if in the vicinity of the osteoid osteoma.

Radiographic Findings

1. Round or oval, usually radiolucent central nidus. The nidus may contain a small central radiopaque core.
2. Perifocal bone sclerosis. Often very slight if the site is in the spongiosa, more pronounced if in the cortex.

There may, however, be considerable variations in this picture of a typical osteoid osteoma, and early lesions in particular may often not be detected by X-ray.

Angiography

Pronounced hypervascularization of the nidus has been demonstrated in angiography by Lindbom, Lindvall & Spjut (1960), a valuable finding for differential diagnosis in relation to osteomyelitis. The nidus is surrounded by a thin, considerably weaker vascularized border zone. Thus in degree of vascularization the osteoid osteoma differs from most other benign tumours. Exceptions are giant cell tumours and meningeomata, among which, accordingly, the osteoid osteomata should be counted from the vascularization aspect.

Histological Picture

The nidus may be classified grossly under two main types with different histological pictures.

1. *Granular and brittle nidus.* The nidus consists of osteoid and bony trabeculae in different proportions in a substratum of heavily vascularized osteogenic connective tissue. The osteogenesis is pronouncedly active and productive. Isolated osteoclasts occur. This type of nidus may be confused with osteogenic sarcoma (Jaffe 1961).
2. *Nidus resembling a firm core.* The nidus consists of closely set trabeculae of atypical new *bone on residual fragments of the original bone*. The intertrabecular spaces contain numerous dilated blood vessels. Osteoblasts and osteoclasts indicate that the bone is in process of reconstruction.

Aetiology and Neoplastic Nature

The aetiology of the *osteoid osteoma is unknown*. Some of the theories relating to the nature and genesis of the osteoid osteoma will be briefly touched upon.

1 *Benign tumour* Most authors agree with Jaffe as regards this theory. Particularly in its later stages of development the osteoid osteoma manifests histological patterns of a pronouncedly neoplastic nature. The osteogenesis is very active with lively production of highly atypical bone in a strongly vascularized and cellular stroma of connective tissue. At this stage the lesion may even be misinterpreted as an osteogenic sarcoma. Jaffe considers that these neoplastic patterns predominate over certain other characteristics which have induced some authors to conceive of the lesion as being of an inflammatory nature.

2 *Hamartoma* Bergstrand (1930) described two cases conforming with osteoid osteoma five years before Jaffe introduced the term. Bergstrand thought it probable that the lesion, which was unknown at the time, was of embryonal nature. This theory has not been accepted by other authors.

3 Boyd (1961) regarded the osteoid osteoma as a reactive lesion which even less than a hamartoma can be regarded as a neoplasm.

4 *Inflammation* This theory is supported by Pines, Lavine & Grayzell (1950) and by Lofgren (1953). Lofgren bases his inflammation theory on certain characteristics and findings which differ from neoplasia.

(*a*) *Pain* This almost constant symptom of osteoid osteoma is more usual in inflammation than in neoplasia. Jaffe, on the other hand, explains the pain by the strange anatomical conditions in the blood supply of the lesion: several arterioles are often lumped together in a small area on the border between the nidus and the surrounding bone tissue. The cause of the typical pain is probably the limitation of the rather large blood supply to a small area contained within rigid walls. Histological studies of the vessels in osteoid osteoma made by Lindbom, Lindvall & Spjut (1960) show that the largest increase in the number of vessels is on the arterial side. In analogy therewith the same authors observed by means of angiographic serial technique that the nidus was very quickly filled with radiopaque medium which only disappeared slowly and gradually. This would imply an increase of pressure on pain nerves through the heavy inflow and poor outflow of blood, resembling the pain mechanism in a hyperaemic dental pulp.

(*b*) The *smallness* and *self limiting nature* of the lesion. Jaffe finds no explanation for this characteristic. The lesion may also disappear spontaneously (Vickers, Pugh & Ivins 1959, Lindbom *et coll* 1960). In our opinion, however, the limited size of a lezion cannot be used as indication either of inflammatory or of neoplastic nature, for one of the signs of a very benign neoplasm is its slow growth.

(*c*) *Histological inflammation* of a chronic nature in Lofgren's material. In our opinion this need not imply that infection was an aetiological factor; it may equally well indicate secondary, aseptic inflammatory changes owing to necrosis caused by changed blood supply conditions (Jaffe 1961, Lindbom *et coll* 1960).

(*d*) *Accumulation of infections* in the health history of Lofgren's patients. These are, however, for the most part very ordinary, banal infections which

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Fig. 1. Fibrous cartilage of the articular surface with irregular jagged surface and hyperplasia in some places. Azan × 30.



Fig. 2. The tumour lying medially in the condyle is without capsule and does not communicate with the [illegible]. The tumour consists of a central nidus with atypical bone formation in a fibrillar stroma and is surrounded by a weak perifocal reactive zone. The articular surface lacks a covering of cartilage in the area of the tumour. Azan × 30.

we consider can hardly be related directly to the genesis of the osteoid osteoma.

5. *Trauma.* In Jaffe's investigations the patients reported a preceding trauma in only 30 per cent of the cases, and only in a small number of the latter is the statement considered credible, so that trauma can probably not *be regarded as an aetiological factor.*

We have therefore considered the objections raised in the literature against Jaffe's theory of *neoplasia to be not well founded and we concur with* Jaffe's views.

Case Report

The patient was a 48-year-old man who at the age of 41 had presented at a provincial hospital for treatment of arthralgia accompanied by dislocation of the right mandibular joint. The health history also included general articular symptoms. The treatment consisted of extirpation of the articular disc and of transplantation from the iliac crest to the articular tubercle. The transplantation was done in order to prevent forward movement of the condyle. The result was initially satisfactory, but despite exercising of the jaw, the extent of movement in the joint was increasingly inhibited. At the age of 48 the maximum jaw opening capacity was 14 mm between the cutting edges of the incisors. Nor was there any alleviation of the pain in the mandibular joint, which became increasingly persistent.

It was decided that a new operation should be made. After exposure of the bone the condyle was found to be almost completely immovable. The articular tubercle was thickened and bridged the joint laterally, probably on account of the earlier bone transplantation. The latter was chiselled off, after which the mobility of the condyle increased and the articular space became visible. The neck of the mandible was exposed and, with the aid of pins, first wires and then a Gigli saw were placed around the neck, which was sawn off. With a wood screw placed in the condyle the latter was dislocated, whereupon the attachment of the pterygoid muscle was ruptured.

Follow-up showed improved function of the mandibular joint and freedom from symptoms.

The extirpated condyle was flattened on the upper side of the articular surface, and the cartilaginous surface in the central parts of the joint was irregular.

The condyle was X-rayed, but without pathological findings, and was then subjected to patho-anatomical examination.

Patho-Anatomical Examination

After decalcification serial sections were made of the condyle in the sagittal plane. The articular surface was only partially covered with fibrocartilage-like tissue which had an irregular, jagged surface and in places was hyperplastic and oedematous and contained vessels with thickened walls (Fig. 1). The bone tissue was of normal appearance in most sections, but in a few of the

a ventral direction But as the disc had been removed after division of the capsule and the tubercle had been traumatized there were great risks of ankylosis especially as it might be expected that the articular cartilage in the condyle was not intact

The original reasons for the patho anatomical examination of the condyle were the preoperative X ray findings and the health history

Conceivable Causes of the Cartilaginous Changes

1 *Rheumatoid arthritis* The occurrence of this disease in the patient s history and the histological findings of destruction of cartilage and formation of granular tissue suggest that the cartilaginous changes may have been of rheumatoid character (Oshrain & Sackler 1955)

2 *Osteoarthritis* (degenerative disease of the joint) This common complaint after the age of 40 cannot be ruled out by the histological findings but can probably not alone have caused the severe clinical symptoms in this case (Shafer Hine & Levy 1958)

3 *Traumatic lesion* (*a*) At the time of the earlier surgical operation This is the most probable cause of the cartilaginous changes (*b*) Some of the deformities in the articular cartilage may also derive from the later operation

4 *The tumour* Dysfunction of the mandibular joint owing to pain from the osteoid osteoma may possibly have contributed to the cartilaginous changes

Differential Diagnosis of the Bone Lesion

The histological picture is on the whole typical of osteoid osteoma but the following lesions are of interest from the point of view of differential diagnosis

1 *Monostotic fibrous dysplasia* The formation of atypical bone in a fibrillar stroma gives the present lesion certain resemblances to fibrous dysplasia The lesion is rather more vascular and cellular moreover than an osteoid osteoma is usually Therefore the picture may possibly lead one to suspect a small localized focus of fibrous dysplasia It is extremely unusual however that the lesions in fibrous dysplasia are so small and well demarcated as in this case (Ringertz 1953)

2 *Solitary enostosis (medullary osteoma bone fleck)* The present lesion bears certain anatomical resemblances to solitary enostosis which histologically however usually shows compact trabeculae of mature lamellar bone Enostoses moreover are generally asymptomatic (Jaffe 1961)

3 *Bone abscess* This may be ruled out since accumulations of inflammatory cells are lacking in the present lesion

Several other diseases may cause bone lesions which histologically are reminiscent of osteoid osteoma for example Paget s disease and hyperparathyroidism and may therefore give rise to a wrong diagnosis Such diseases however can be readily excluded from the differential diagnosis if the remaining symptoms are absent as in this case

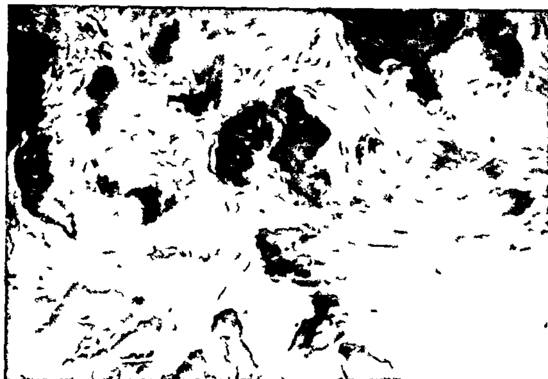


FIG. 3. Formation of atypical non-lamellar bone trabeculae. The intertrabecular spaces are filled with fibrotic connective tissue. The fibres are yellow stained (not genuine collagen). Hansen × 480.

medial sections a rounded tumour-like formation of about 3 mm diameter was discovered near the articular surface, which here was without cartilaginous covering (Fig. 2). The tumour had no capsule and did not communicate with the cortex. The tumour consisted of a central nidus with closely packed pulpy trabeculae of atypical bone which in spots were strongly stainable with haematoxylin. Osteoclasia and new bone formation occurred in mutually adjacent areas separated by dark demarcation lines ("pagetoid" structure). The intertrabecular spaces were filled with moderately vascularized fibrous connective tissue with a moderate content of connective tissue cells (Fig. 3). The fibres probably did not consist of genuine collagen, for they stained yellow in Hansen and red in Azan. The nidus was surrounded by a narrow zone of rather more compact bone than in the other parts of the condyle, but with otherwise normal bone picture (perifocal reactive zone). In the boundary region between this bony zone and the actual nidus there were several large channels filled with erythrocytes.

There was no specific inflammation or malignant transformation of tissue. The findings suggest degeneration of the articular cartilage tissue and osteoid osteoma.

DISCUSSION

That the removal of the articular disc did not rectify the dislocation is natural. The building up of the articular tubercle with bone transplant constitutes an effective obstruction to too great excursions of the condyle in

a ventral direction But as the disc had been removed after division of the capsule and the tubercle had been traumatized, there were great risks of ankylosis especially as it might be expected that the articular cartilage in the condyle was not intact

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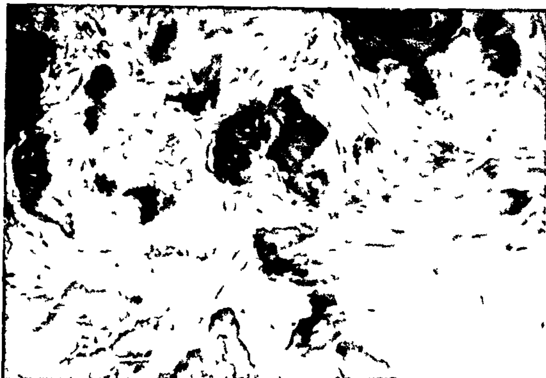


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DISCUSSION

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ON LARYNGOCELE

AAGE MUNK JENSEN and UGGI SAMUELSEN
Nykøbing F., Denmark

From the Department of Otolaryngology (Head: K. Faaborg Andersen, M.D.) and the Department of Radiology (Heads: K. Lubschitz, M.D., and V. Westergaard Nielsen, M.D.), The Central Hospital, Nykøbing F.

After reviewing the occurrence, aetiology, pathogenesis, diagnosis and treatment of laryngocele, the authors report a case of mixed, unilateral laryngocele in a 63 year old man.

The first to recognize the presence of a laryngocele seems to have been Abulcasim in the 11th century. Subsequently it was described by several authors (for example Paré and Ploter) but the first detailed description was by Napoleon's army surgeon Larrey (1829). During the Egyptian campaign he observed the disease in the muezzins, the Mohammedan criers of the hour of prayer from the tops of the minarets. Larrey called the condition "goitre aerien ou vesiculaire". In 1867 Virchow described the pathology of what he called laryngocele ventricularis.

Laryngocele is fairly uncommon. Robert Lund in 1939 collected a total of 60 cases from the literature and Videbech in 1941 60–70. According to Johnston less than 70 had been observed up to 1953, while in 1959 Forrester mentions 90 and Borsanyi in 1961 about 100 cases, stating that nearly half had been observed within the past decade. In 1961 Fredrickson stated that 174 cases were on record. Several others have found values of the same order of magnitude, whereas Grimaud (1960) mentioned a considerably larger number, viz. about 300.

Laryngocele or anatomically more correctly a laryngeal ventriculocele (*Czeizel & Fabries* 1960) is an abnormal dilatation of the ventricular appendix. During foetal life and the first years of life the appendicular structure is relatively well developed, but subsequently it diminishes quite considerably in relation to the ventricle of Morgagni, presenting itself only as a slight bulging of the latter, not reaching beyond the upper edge of the thyroid cartilage. In a few per cent, however, the appendix persists as a fairly large structure (Comino). It is furnished with numerous mucous glands which lubricate the larynx.

The anthropoid ape has large air sacs corresponding exactly to the laryngoceles. Some authors believe that these air sacs are of phonetic significance, while Negus concludes that "the sum total of evidence seems to me to be strongly against a vocal and in favour of a respiratory function for air sacs".

Generally the laryngoceles are classified into an internal, an external and

ZUSAMMENFASSUNG

Hier wird ein Fall von Osteoid Osteoma im Caput mandibuli beschrieben, eine Lage, die in der Literatur früher nicht berichtet ist

Es handelte sich um einen 48jährigen Mann, der ein ankylotisches Kiefergelenk mit Arthralgie hatte Die Symptome zeigten Rezidive trotz Bewegungstherapie Deshalb wurde der Caput mandibuli amputiert, wobei ein Osteoid Osteoma im Präparat gefunden wurde Keine Veränderungen konnten im Röntgenbild beobachtet werden

In dem Aufsatz wird die Literatur über Osteoid Osteoma durchgegangen und diskutiert, mit besonderer Rücksicht auf die Genesis Die Pathogenesis des Ankylosis wird mit Rücksicht auf frühere Behandlung diskutiert, und die Methodik der aktuellen Operation wird beschrieben

Im Anschluss an die histopathologische Beschreibung werden die möglichen Ursachen der Knorpelschaden diskutiert, ebenso wie der eventuelle Zusammenhang zwischen den Knorpelschaden und dem Osteoid Osteoma, und die Differentialdiagnose des Osteoid Osteomas

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Royal School of Dentistry Stockholm Sweden

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several additional cases so he emphasizes that the percentage must have been higher The laryngocele need not be caused by the tumour invasion as such as unilateral tumours may coexist with bilateral or contralateral laryngocele On the other hand the tumour invasion appears to cause alterations of pressure in the larynx and thereby give rise to laryngocele The same causal relationship was stated by Nucci who also like others mentions the possibility that a laryngocele may be carcinogenic owing to the chronic irritation Possibly the cancer and the laryngocele may mutually accelerate each other

External laryngoceles manifest themselves only as an air filled tumour on the side of the neck and an occasional belching sound owing to expulsion of air from the laryngocele caused by contraction of the pharyngeal constrictors It is rarely associated with headache owing to compression of the cervical vessels Internal and mixed laryngoceles may cause the following additional signs Alteration of the voice in the form of a peculiar timbre hoarseness or aphonia dyspnoea cough dysphagia and a sensation of a foreign body in the throat Lastly infected laryngoceles may give rise to pain and fever and all the symptoms and signs of an abscess The severity of the symptoms is extremely varied and some cases are symptom free On the other hand a laryngocele may develop within a short time into an alarming condition of airway obstruction possibly due to aspiration of pus from a laryngopyocele

To arrive at the correct diagnosis it is most important as in all rare diseases to bear the condition in mind Laryngoscopy shows in cases of internal and mixed laryngocele a bulging of the false cord possibly extending to the ary epiglottic fold and in the event of larger laryngoceles past the pyriform sinus and the vallecula leading to a major or minor displacement of the epiglottis Frequently the homolateral vocal cord may be hidden from view and occasionally the laryngocele may almost completely prevent the passage of air The mucosa overlying the intumescence is smooth not ulcerated X rays are of great help possibly with percutaneous injection of contrast medium into the laryngocele sac Tomography is excellent for visualizing the size and shape of the laryngocele showing also fluid content if any Films taken while the patient performs Valsalva s manœuvre may disclose laryngoceles which cannot be detected on ordinary films In this connection however it must be pointed out that during this manœuvre normal persons also show a certain bulging of the hypopharyngeal wall which is apt to be mistaken for a laryngocele as not even tomography can always demonstrate the communication to the larynx After oral administration of a contrast medium the bulge will be filled with contrast medium if it issues from the hypopharynx while a laryngocele does not fill Lelisati (1958) using X ray examination including tomography during forced expiration or phonation of the vowel e found among 100 patients with chronic laryngitis 20 per cent having translucencies which were interpreted as laryngoceles No further efforts seem to have been made to confirm the diagnosis especially no X rays after oral administration of contrast medium and one cannot help suspecting that a number of the

a mixed combined internal–external type. The laryngocele is said to be internal if it is situated deep to the thyroid membrane, external if it is superficial to this membrane, while the mixed type is inside as well as outside the membrane. The most common site of perforation is at the entry of the superior laryngeal artery. According to some workers (Harrison 1950) the laryngocele does not pierce the membrane but proceeds behind it. The most common type is the mixed laryngocele, while the internal variety is rare (Issa *et al.* 1961). A few authors, however, state that the internal type is most common (Boisanyi 1961). Very often the laryngocele is bilateral and in that case it may be of two different types. Trapnell found bilateral involvement in about 30 per cent of all cases. The wall of the laryngocele is lined with respiratory epithelium but may have islets of squamous epithelium. The stroma contains mixed mucous and serous tubular glands. In general the laryngoceles are pneumoceles but may also be of the mucocele or pyocele type. The latter are reported to make up about 10 per cent (Lund 1939, Videbech 1941), and this accords with Glatz' (1961) finding of eight such cases on record. Directly this complication might be imagined to be more common as the laryngoceles affect a region which is greatly exposed to infection. According to Glatz the explanation why nevertheless laryngopyoceles are so uncommon may be partly the intralaryngeal bulge pressing on the narrow entrance to the laryngocele and partly in external and combined types the pressure of the cervical muscles which are apt to milk back any septic material into the larynx.

Laryngocele is rare in women, about 90 per cent of the patients being men. The age of predilection is the fifties; half the patients have been between 50 and 60. The condition is considered most common among orientals, possibly because of their guttural speech.

The aetiology is not completely elucidated but it is generally agreed that an increased intralaryngeal pressure is an important factor. Such an increase in the pressure may be induced by disorders such as chronic bronchitis, other forms of persistent cough or straining at stool. Occupational factors are also in evidence, glass and wind instrument blowers, singers, commanding officers and others abusing their voice being particularly exposed. Another significant factor is no doubt a weakness of the laryngeal tissue, congenital or acquired. As already mentioned a few per cent show an enlarged ventricular appendix which may also predispose to laryngocele. Lastly an alteration of the current of air, e.g. in scar formation and following paralysis, may be of importance. The growth of the laryngocele may be furthered by a valvular action caused by a valve formation at the entrance which admits the air to the laryngocele but prevents its escape.

A problem apart which has been discussed by several authors is the relation between laryngocele and laryngeal cancer. According to Leborgne laryngocele is present in 10.15 per cent of patients with laryngeal cancer. Among 517 cases of laryngeal carcinoma Pietrantoni found X-ray evidence of laryngocele in 6 per cent, while examination of operative specimens revealed



Fig 1 A right sided mixed external internal laryngocele

During the past two years increasing hoarseness and dyspnoea For a year cough productive of purulent sputum During the past three years the patient had been working as a watchman on the rails, and this had involved much shouting and blowing a bugle

On admission he was dyspnoeic and slightly cyanosed In the right carotid triangle there was a swelling almost as large as a hen s egg which could be partially compressed He had a very hoarse and striking voice, almost ventriloquial Laryngoscopy revealed a large, round smooth bulge involving the right false cord and the pyriform sinus, displacing the epiglottis and obscuring the right true cord It had obliterated almost the entire laryngeal space as there remained only a narrow semilunar chink on the left X rays revealed an air filled cavity, the size of a tangerine, on the right supero laterally to the larynx and a walnut sized also air filled cavity at the site of the false cord extending beyond the midline (Fig 1) Tomography gave an impression of an air filled, narrow canal extending towards the sinus of Morgagni (Fig 2)

Percutaneous puncture was followed by severe emphysema with further respiratory embarrassment requiring tracheotomy A few days later the

translucencies have been pharyngeal bulges Percutaneous or intralaryngeal puncture may also be of diagnostic significance Pressure upon the tumour may occasionally make it disappear with a characteristic sound

Laryngocele or *laryngopyocele*, may be confused with other conditions Inflammatory conditions (e g tuberculosis, syphilis diphtheria and typhoid fever) may give rise to necrosis of the laryngeal cartilages and thereby an air sac known as laryngocele spuria However, these structures are generally close to the midline A branchiogenic cervical cyst a dermoid cyst or an aberrant thyroglossal cyst may also present an appearance very similar to that of a laryngocele (Herberts 1957) Simple abscesses on the neck and para pharyngeal abscesses may be confused with laryngopyocele

A laryngocele does not always require treatment Small silent laryngoceles need no direct treatment but possible eliciting factors should be eliminated (Jackson 1947) In rare cases a laryngocele has been reported to disappear spontaneously (Beck & Schneider 1928) The most important operative indications are respiratory trouble hoarseness dysphagia a risk of undetected cancer infection occupational handicap and cosmetic reasons

As a rule the treatment is surgical removal and to our knowledge there have been no instances of recurrence after operation It is generally agreed that external and mixed laryngoceles should be approached from the outside As far as internal laryngocele is concerned opinions are divided Some authors (Herberts 1957 Grimaud 1960) feel that this variety should be approached also from the lateral aspect while others (Jackson 1947 Butler 1950) have used endolaryngeal operation usually with cauterization Borsanyi recommends the former method in cases of large internal laryngoceles and the latter in smaller ones Lastly several authors (Czeizel & Fabrics 1960) have suggested operation through a laryngo fissure

A few authors (Aubry Senechal *et al* 1953) have successfully used injection of 10 per cent trichloracetic acid into the laryngocele sac This induces a sterile inflammation which eventually makes the sac collapse This may take three or four weeks A 10 per cent sodium hydroxide solution has also been used for this purpose However most workers advise against this treatment as it may be dangerous or inadequate Laryngopyoceles in the acute stage should be treated with incision and drainage and with excision in a quiescent stage (Boussens 1961 Kiel orian 1962) Tracheotomy may of course be required if the laryngo(pyo)cele gives rise to a dangerous airway obstruction and occasionally tracheotomy has to be done in the course of the operation

The prognosis of uncomplicated laryngocele must be considered good while for laryngopyocele it is poorer and fatal cases are on record

Present Case

A 63 year old railway worker who had always been in good health apart from renal gravel During the past three years before admission he had noticed a swelling on the right side of his neck varying in size but slowly growing



Fig 4 Follow up X ray 12 days after the operation taken during Valsalva s manœuvre

laryngocele was excised under general anaesthesia Through an oblique incision on the right side of the neck the laryngocele sac was mobilized from the bottom through the thyrohyoid membrane as far as the pedicle which was ligated

In its collapsed state the removed specimen measured about 4 × 6 cm (Fig 3) Histological diagnosis stratified columnar epithelium with cilia some inflammatory reaction in the tunica propria

Postoperative course uneventful The tracheal cannula was left for 10 days in order to relieve the larynx after the operation X rays 12 days after the operation showed completely normal appearances on both sides on the ordinary films but during Valsalva s manœuvre there was a bilobular air cavity as large as a hen s egg on the left side of the larynx (Fig 4) This cavity looked like a laryngocele but tomography during Valsalva s manœuvre showed no communication to the larynx and administration of contrast medium distinctly set out the cavity so it must represent a bulging from the pharynx (Fig 5) On the right there was no longer any laryngocele only a very slight bulging of the hypopharynx far smaller than on the left presumably caused by cicatricial changes



Fig. 2. Tomographic appearance of the laryngocele. A narrow, air-filled canal to the sinus of Morgagni can be barely discerned.



Fig. 3. The removed laryngocele in a collapsed state.

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The Central Hospital Nykøbing F Denmark



Fig. 5. Postoperative X-ray during Valsalva's manœuvre after oral administration of contrast medium.

On discharge the patient was feeling well, and his voice was entirely normal. Laryngoscopy showed the right false cord to be very slightly prominent to the posterior aspect. Otherwise, the appearances were normal. Out-patient follow-up, two months after discharge, still showed a slight swelling of the right false cord far posteriorly, but otherwise the appearances were completely normal, as on discharge, and the voice was satisfactory.

ZUSAMMENFASSUNG

Eine Übersicht über das Vorkommen, die Ätiologie, die Pathogenese, die Diagnostik und die Therapie des Laryngozeles wird gegeben. Danach wird ein Fall von gemischtem, einseitigem Laryngozele bei einem 63jährigen Mann mitgeteilt.

RÉSUMÉ

On a commencé par vous donner un aperçu de l'apparition et la fréquence du laringocèle, son aétiologie, sa pathogénèse, sa diagnose et sa thérapie. Après, on étudie un cas de laringocèle mixte et unilatéral d'un homme de 63 ans.



Fig 1 Low power view of a frozen section of the decalcified inner ear Sites of succinic dehydrogenase activity in the crista ampullaris (C) stria vascularis (SV) spiral ligament (SL) spiral ganglion (G) organ of Corti (OC) and Eustachian tube (E) are dark blue (black on the photograph) ×13

The decalcified tissue blocks were briefly blotted on filter paper and frozen on dry ice The blocks were sectioned on a rotary microtome at 16 μ in a cryostat at 18°C The plane of sectioning was chosen so that the cross sections of the posterior crista ampullaris and the macula sacculi were obtained together with midmodiolar sections of the cochlea (Fig 1) The sections were placed on coverslips thawed and dried at room temperature for 30 minutes Following this the slides were incubated at 37°C aerobically in one of several substrate solutions

Cytochrome oxidase activity was demonstrated by using p aminodiphenylamine as a substrate in conjunction with Naphthol AS L3G (Burstone 1960) Control sections were incubated in media to which KCN (0 2 mg/ml) was added as an inhibitor

Succinic dehydrogenase reduced diphosphopyridine nucleotide (DPNH) diaphorase malic dehydrogenase, lactic dehydrogenase glutamic dehydrogenase dihydrolipoic dehydrogenase reduced triphosphopyridine nucleotide

METABOLIC PATHWAYS IN THE VESTIBULAR LABYRINTH AS REVEALED BY HISTOCHEMICAL TECHNICS

YASUYA NOMURA and KÁROLY BALOGH, JR
Boston, Mass., U S A

From the Department of Otolaryngology (Head Prof H F Schuknecht), Massachusetts Eye and Ear Infirmary, and the Department of Pathology, Harvard Medical School, and the James Homer Wright Pathology Laboratories (Head Prof B Castleman) Massachusetts General Hospital, Boston

Tissues of the vestibular system were studied for the activity of a number of oxidative enzymes by using histochemical methods In general, striking activity was found in the sensory epithelium of the crista ampullaris and macula sacculi, while other parts of the membranous labyrinth showed varying degrees of enzyme activity A detailed description of the observations is presented The results indicate a marked capacity of the sensory epithelium for anaerobic glycolysis, the presence of a citric acid cycle and active hexose monophosphate shunt, the existence of the cytochrome oxidation system and the capacity of oxidative decarboxylation of alpha keto acids to energy-rich acyl coenzyme A The significance and possible relation of these metabolic avenues to the function of the cells is discussed briefly It is presumed that physiological stimuli and toxic agents affect the sensory epithelium by interfering with its complex metabolism

INTRODUCTION

As the result of the development of histochemical technics suited to the study of bone and hence of bone-embedded structures it seemed possible that new insight into the metabolism of the cells of the vestibular receptors might be gained by the application of these technics to the crista ampullaris and macula sacculi of the guinea pig

MATERIAL AND METHODS

Twenty five young adult albino guinea pigs were studied in the course of this work The animals were decapitated under ether anesthesia and their tympanic bullae removed and opened After trimming off excess bone and soft tissue the blocks consisted of the unopened cochleae and vestibular systems These blocks of tissue were decalcified for 96 hours at 4°C with 10 % Versene solution at pH 7 4 as described earlier (Balogh 1962) Polyvinylpyrrolidone in a final concentration of 5 %, added to the decalcifying solution, resulted in better preservation of tissue

This study was supported by Research Grant NB 04155 01 from the National Institute of Neurological Diseases and Blindness National Institutes of Health of the United States Public Health Service

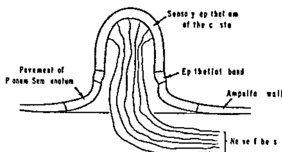


Fig 2 Zones of the crista ampullaris

Distinct quantitative and qualitative differences were noted in the enzyme pattern of various zones as summarized in Table 1

Striking activity of DPNH diaphorase (Fig 3) TPNH diaphorase glucose 6 phosphate dehydrogenase dihydrolipoic dehydrogenase isocitric dehydrogenase lactic dehydrogenase and malic dehydrogenase were seen throughout the sensory epithelium except for its basal portion which appeared to show less diformazan deposition The sensory epithelium also showed slight

Fig 3 Distribution of DPNH diaphorase activity in the posterior crista ampullaris and ampullar wall (right upper corner) 160

TABLE 1. *Crista ampullaris*

	Incubation time (min)	Sensory epithelium	Epithelial band	Pavement of planum	Ampullar wall
Cytochrome oxidase	15	+ + + +	+ +	+	+
Succinic dehydrogenase	60	+	0 ±	+ +	+
DPNH diaphorase	10	+ + +	+ + +	+ +	+
Malic dehydrogenase	10	+ + +	+ +	+ +	
Lactic dehydrogenase	30	+ + +	+ +	+ + +	+
Glutamic dehydrogenase	75	0–±	0	0	±
Dihydrolipoic dehydrogenase	25	+ + +	+ + +	+ + +	+
TPNH diaphorase	30	+ + +	+ + +	+ +	
Isocitric dehydrogenase	60	+ + +	+ +	+ +	+
Glucose-6-phosphate dehydrogenase	30	+ + +	+ +	+ +	+

(TPNH) diaphorase, isocitric dehydrogenase and glucose-6-phosphate dehydrogenase activity were demonstrated as described elsewhere (Balogh, Dudley & Cohen 1961, Balogh in press). The incubation time was modified (as indicated in Table 1) for better demonstration of the reaction. In all instances the specific dehydrogenase catalyzes the transfer of electrons from the substrate to the specific pyridine nucleotide, from which in turn they are transferred by a diaphorase to a ditetrazolium salt, Nitro BT, the final electron acceptor. Thus various dehydrogenase-diaphorase systems are demonstrated histochemically. When DPNH and TPNH were used as substrates, the respective diaphorases were visualized directly. Nitro BT is readily reduced to a deep blue granular, fat and water insoluble substantive diformazan which serves as an indicator of the site of enzyme activity (Pearse 1961). Control sections were incubated in media otherwise complete from which the specific substrate was omitted.

RESULTS

In all cells diformazan precipitate was found only in the cytoplasm; nuclei and ground substance remained consistently negative. Control sections failed to show any reaction. In an attempt at objective evaluation, the reactions were graded arbitrarily zero to four plus.

Crista ampullaris

The epithelium of the area of particular interest to us was divided anatomically into four zones (nomenclature of Borghesan 1962) (Fig. 2):

(1) sensory epithelium of the crista ampullaris
(2) epithelial band around the crista
(3) pavement epithelium of the planum semilunatum
(4) epithelial lining of the ampullar wall



Fig 3 Strong cytochrome oxidase activity is present in the crista ampullaris and its nerve fibers ×18

The sensory epithelium of the macula showed the most marked activity of all layers (Table 2) In the undifferentiated epithelium adjacent to the macula, almost the same degree of DPNH diaphorase malic dehydrogenase and lactic dehydrogenase activity were seen as in the sensory epithelium, but cytochrome oxidase succinic dehydrogenase, TPNH diaphorase, isocitric dehydrogenase,

TABLE 2 *Macula sacculi*

	Sensory epithelium	Epithelium surrounding macula	Saccular membrane	Connective tissue cells under the macula
Cytochrome oxidase	+ +		+	
Succinic dehydrogenase			−	±
DPNH diaphorase				
Malic dehydrogenase				
Lactic dehydrogenase				
Glutamic dehydrogenase	+	0	0	0
β-hydroxybutyric dehydrogenase				
TPNH diaphorase				
Isocitric dehydrogenase				
Glucose 6 phosphate dehydrogenase				+



FIG. 4. Relatively weak succinic dehydrogenase activity is demonstrated in the sensory epithelium. There is almost no reaction in the epithelial band (arrow) but the pavement epithelium reacted moderately. × 210

succinic dehydrogenase (Fig. 4) but practically no glutamic dehydrogenase activity. Cytochrome oxidase activity, while marked in the sensory epithelium (Fig. 5), diminished somewhat in the epithelial band and in the pavement; it was considerably decreased towards the ampullar wall. No other differences could be recognized in the cell population of the sensory epithelium. The cupula was not present in any of the specimens.

The epithelial band showed essentially similar enzymatic activity compared to that of the sensory epithelium, except that minimal succinic dehydrogenase activity could be detected (Fig. 4). The pavement of the planum semilunatum showed moderate, and the epithelial lining of ampullar wall disclosed only slight activity of all enzymes that were found prominently active in the sensory epithelium.

Macula sacculi

The sacculus was likewise divided microscopically into four zones (Fig. 6):

(1) sensory epithelium
(2) undifferentiated epithelium surrounding the macula
(3) saccular membrane
(4) connective tissue cells under the macula

for the utilization of glucose in the citric acid cycle and of the hexose monophosphate shunt. The histochemical demonstration of dihydrolipoic dehydrogenase activity indicates that these cells also have the ability to use oxidative decarboxylation of alpha keto acids in order to form energy rich acetyl coenzyme A and succinyl coenzyme A, respectively. It is well known that most dehydrogenases will not transfer hydrogen from a substrate directly to oxygen but cytochrome oxidase will couple with the dehydrogenase systems as well as with molecular oxygen. For this reason the demonstration of marked cytochrome oxidase activity in the sensory epithelium is of considerable importance since it indicates the presence of a complete mechanism for the direct consumption of oxygen. Less abundant enzyme activity at the base of the sensory epithelial cells may have its explanation in the simple fact that this area is mainly occupied by the nuclei of supporting cells (Wersäll 1956).

The methods employed in the present study are considerably different from those of previous investigators who incubated the whole membranous labyrinth with substrate solutions for the demonstration of cytochrome oxidase and succinic dehydrogenase (Koide 1958, Vinnikov 1958, Imokawa 1959) as well as other enzymes of the citric acid cycle (Koide 1958, Imokawa 1959). These investigations have led to heavy dye precipitation only on the surface of the crista ampullaris raising the question of insufficient penetration of the substrate solution. In the earlier studies a less suitable indicator, neotetrazolium, was used which has a tendency to crystal formation in tissues (Pearse 1961). Therefore it is difficult to compare critically the results obtained by various methods. However, technical inadequacies in this study as a possible cause of low succinic dehydrogenase activity appears unlikely because osteoclasts in the same sections demonstrated the usual strong enzyme activity. It seems likely that the sensory epithelium of the crista ampullaris and macula oxidizes succinate via specific dehydrogenase at a relatively low rate. Analogous differences in the rates of activity of this and various other enzymes involved in glucose metabolism do exist and also have been quantitatively measured in a number of other normal tissues (von Fellenberg, Eppenberger, Richterich & Aebi 1962).

Recent autoradiographic (Dohlman 1960) and electronmicroscopic (Bairati & Iurato 1960) investigations suggest that the planum semilunatum has a secretory role. The enzymatic activity in the cells constituting the pavement of the planum semilunatum is considerably more prominent than in the adjacent epithelial band or ampullar wall, but unfortunately no conclusions in regard to such function may be drawn from this observation.

On the other hand it can be presumed that physical and biochemical stimuli reaching the sensory epithelium may affect its active metabolism and as a result alter cell function physiologically. The extreme sensitivity of the vestibular receptors to certain types of abnormal stimuli also could be explained by their adverse influence upon the metabolism of the sensory epithelial cells. Further experimental investigations along these lines appear promising and might supply evidence for this.

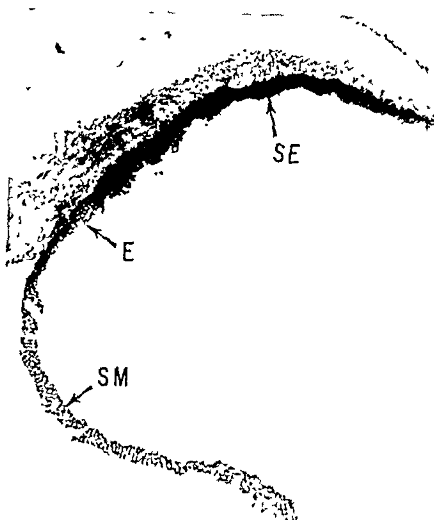


FIG. 6. Glucose 6 phosphate dehydrogenase activity in the macula sacculi. The sensory epithelium (SE) shows marked diformazan deposition, the undifferentiated epithelium surrounding the *macula* (E) and the saccular membrane (SM) are diminishingly active. × 130

glucose 6 phosphate dehydrogenase and dihydrolipoic dehydrogenase were only moderately active. The saccular membrane reacted weakly except for moderate lactic dehydrogenase activity.

Tissues of the macula utriculi, which could be seen in some specimens, reacted similarly to those of the *macula sacculi*.

DISCUSSION

It is apparent from the results of this study that the distribution of oxidative enzyme activity in the vestibular labyrinth follows closely the *normal histological* classification of its epithelial lining. Therefore, the recognition of distinct zones seems justified on the basis of metabolic as well as of morphologic characteristics. These histochemical results suggest that the sensory epithelium of the crista ampullaris and of the macula have ample capacity

GELLE TEST WITH BÉKÉSY AUDIOMETRY

IV Findings in Otosclerosis

GODFREY E ARNOLD and PETER SCHINDLER
New York City N Y, U S A

From the Research Department New York Eye and Ear Infirmary, New York

Three preceding papers on the audiometric Gellé test were devoted to the discussion of method and procedure, normal values as well as the findings in salpingitis Observations on otosclerotic patients are reported in the present study As an essential finding it could be confirmed that otosclerosis abolishes the threshold shift when the effect of altered meatal air pressure is measured by bone conduction In contrast air conduction behaves in a more regular manner, continuing to respond to the pressure changes Comparing the findings of the Gelle test by AC and BC three prototypes of abnormal results could be distinguished They appear to reflect the following conductive lesions slight to moderate ossicular fixation complete fixation as well as the combination of stapedial fixation with tubal obstruction

Confirmation of Previous Findings

After having experimented with the technique of the audiometric Gellé test (Arnold & Schindler 1963*b*) and the normal values obtained in this manner (Arnold & Schindler 1963*c*) we reported the findings in cases of salpingitis (Arnold & Schindler 1963*c*) It is the purpose of the present study to discuss the characteristic responses in otosclerosis To begin with it could be seen in the test results of our first 50 cases that otosclerosis gives a more or less normal response with air conduction (AC) whereas bone conduction (BC) is not influenced by the meatal pressure changes As with any other audiologic test numerous intermediate results may be obtained which reflect the graduated steps from a normal state to the severe auditory limitation in advanced cases of otosclerosis

During these preliminary studies it became apparent that our present procedure is limited by the physical characteristics of the equipment used It has been shown in the first two papers (Arnold & Schindler 1963*a* 1963*b*) that the frequency response of the Beyer insert phone is that of a typical hearing aid transducer Characteristically it shows a rising curve from 100 to 500 cps being deficient for the low frequencies that are most affected by meatal pressure variations

It will be the task of a commercial audiometer manufacturer to construct

This study was aided by The John A. Hartford Foundation of New York

ZUSAMMENFASSUNG

Eine Anzahl oxydativer Enzyme bzw Enzymsysteme konnte in den Geweben des Vestibularorganes histochemisch dargestellt werden Besonders ausgeprägte Enzymaktivität war in den Sinneszellen der Crista ampullaris und der Macula sacculi festzustellen, hingegen wiesen die untersuchten Enzyme in anderen Zonen des Epithelsaumes im vestibulären Labyrinth verschiedene Aktivitätsgrade auf Die ausführlich beschriebenen Beobachtungen sprechen für die Fähigkeit des Sinnesepithels und anderer Zellen im häutigen Labyrinth zum Glucoseabbau sowohl durch anaerobe Glykolyse und Citratcyclus als auch durch den Pentosephosphat Cyclus Die Gegenwart von Cytochromoxydase in den Geweben ermöglicht eine direkte Reaktion der Abbauprodukte mit dem molekularen Sauerstoff Die Funktion der histochemisch lokalisierten Dihydrolipoinsäure-Dehydrogenase besteht in der Bildung von energiereichen Acyl-Koenzym-A-Derivaten durch oxydative Decarboxylierung von alpha-Ketosäuren Die genannten Stoffwechselwege der Glucose stehen vermutlich in engster Verbindung mit der physiologischen Tätigkeit des Vestibularorganes sowie mit seiner Beeinflussbarkeit durch toxische Stoffe

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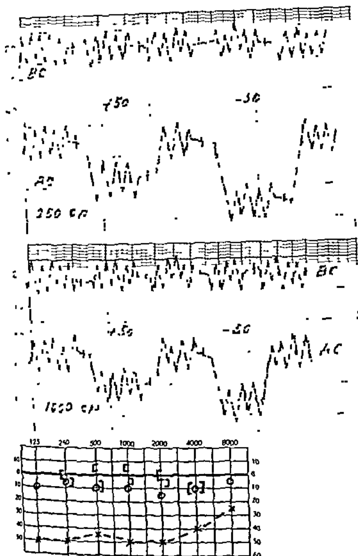


Fig 1 Typical negative Gellé test in a case of unilateral otosclerosis Note air bone gap and absence of BC response to altered meatal pressure despite normal TTS with AC

of TTS by AC than the better right ear Both ears were operated on within one year The right footplate was completely fixed, while the left stapes was visibly overgrown by otosclerotic bone to an even greater degree

There were some cases in which not only the BC curve, but also the AC curve failed to reveal a *significant* TTS in response to altered pressure Fig 3, for example, shows but a small shift of 5–6 db at 250 cps with +50 cm H_2O pressure, and none with —50 cm Testing the same right ear at 1000 cps, +50 cm pressure was ineffective, while —50 cm improved the threshold by about 10 11 db

a pressure capsule containing an AC phone with a response close to the audiometric zero line, at least for the frequencies from 100 to 1000 cps. With our present pressure capsule it is not possible to perform the Gellé test at the most suitable lowest frequencies in cases of marked hearing loss. Since the range of insensitivity of the phone is added to the patient's hearing loss, the remaining audiometric intensity range at the low frequencies is too narrow to permit the recording of a temporary threshold shift (TTS) in response to altered meatal air pressure.

Typical Findings in Otosclerosis

From the large number of our audiometric recordings, a few representative and well recorded cases have been selected for demonstration of the salient features. Fig. 1 shows the audiogram (below) and the audiometric Gellé test (above) in a case of unilateral otosclerosis (female, age 26). Testing at 250 cps, the air–bone gap is about the same as in the audiogram. Positive and negative pressures of $\pm$ 50 cm H_2O were applied in the following sequence: 0, +50, 0, −50, 0. The bone conduction (BC) curve remained completely unaffected. The same pressures were then used with air conduction (AC) showing the typical response to a marked and regular degree. Next, the test was carried out at 1000 cps in the same manner. Without doubt the BC curve failed to respond to the pressure changes, while the AC curve shifted in a normal manner. It is also seen that the low frequency of 250 cps is more affected by altered pressure than the higher tone of 1000 cps. As is normal, negative pressure is more effective than its positive equivalent.

This is a typical Gellé test result in otosclerosis. During subsequent operation, the stapes was found rigidly fixed by otosclerotic bone. Tested again a few weeks later, the air–bone gap appeared closed and hearing was greatly improved. It is noteworthy that the good right ear performed a normal Gellé test with clear TTS by both AC and BC.

Fig. 2 illustrates a case of advanced bilateral otosclerosis. The air–bone gap is clearly evident, though to a lesser degree than in the audiogram. It should be recalled that the readings obtained with our present equipment represent relative values. They must be corrected by the calibration factors discussed in the first two papers (Arnold & Schindler 1963*a*, 1963*b*). Testing both ears at 500 cps, no TTS occurred with BC. In pathognomonic contrast, AC shifted in a regular manner.

Repeated several times, the TTS from $\pm$ 50 cm H_2O pressure were about the same when each ear was re-tested. Hence, these differences between the amounts of TTS with AC obtained of either ear appear to be significant. The right ear showed a TTS of 25 db with −50 cm H_2O, while the left ear shifted by only 15 db with the same pressure. It cannot be stated yet whether this difference of 10 db between the TTS of each ear, and the 10 db difference of the pure tone thresholds at the same frequency of 500 cps, is a coincidence. All that can be said is that the more afflicted left ear revealed a lesser amount

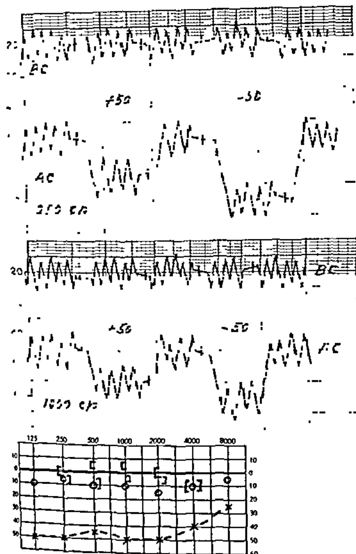


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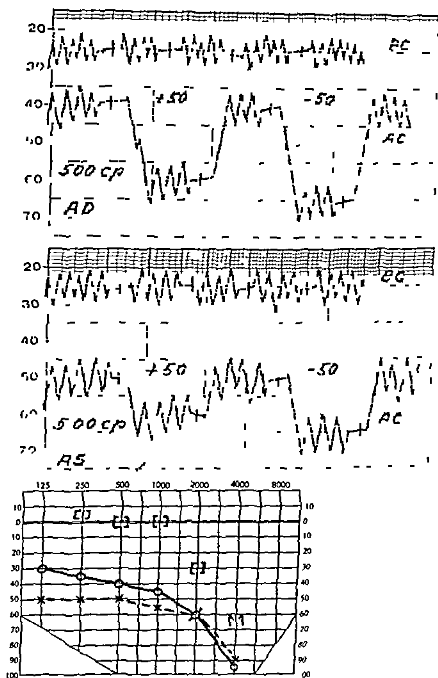


FIG. 2. *Typical Gellé test result in otosclerosis suggesting complete fixation of the stapes in both ears.* It is interesting to note that the binaural difference in the amount of TTS from −50 cm H_2O pressure coincides with the audiometric difference at the same frequency, both being 10 db.

The same patient's left ear responded as shown in Fig. 4. Again there is *no response to altered meatal pressure by BC*, as is characteristic of otosclerosis. Testing AC at *250 and 1000 cps*, AC *shifts slightly with positive pressure but not with negative pressure*. These findings are reminiscent of the results encountered in salpingitis. At operation, about half a year apart, both stapedes *were found solidly fixed.*

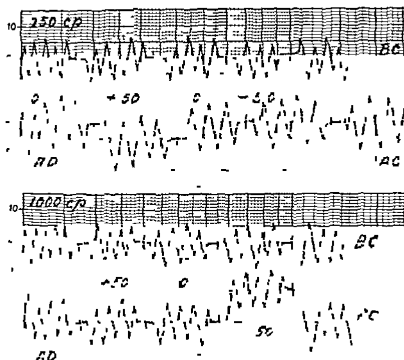


Fig. 3 Gelle test characteristic of otosclerosis inasmuch as BC does not respond to altered meatal pressure In contrast to the Gellé test findings in other cases of otosclerosis AC also shows little TTS with altered pressure in this patient's right ear (comp Fig 4)

Otosclerosis and Salpingitis

It is well known in clinical practice that certain otosclerotic patients derive benefits from tubal inflation On this clinical experience was based the practice of caring for otosclerotic patients by the old methods of tubal inflation so called pneumo massage or keeping nasal respiration free As can be demonstrated by audiometric measurements inflation of obstructed ear tubes may improve the hearing threshold by as much as 10 db Now if a patient with a combined otosclerotic and tubal hearing loss of 40 db finds his hearing level shifted to 30 db following tubal inflation he will experience a definite improvement of serviceable hearing

The following case referred by J Swift Hanley M D illustrates this point A man aged 53 suffered from bilateral otosclerosis He stated that self inflation improved the hearing in his left ear Fig 3 demonstrates his Gelle test findings In the upper portion the reactions of the right ear are shown It is obvious that BC suggests fixation of the stapes while AC responds promptly to positive and negative meatal pressure the latter being slightly more effective This is a typically negative Gelle test characteristic of otosclerosis

In the lower section of Fig 3 the Gelle test response of the left ear is shown

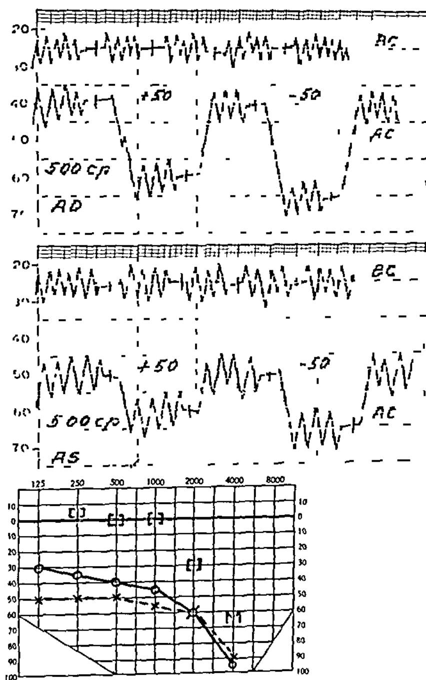


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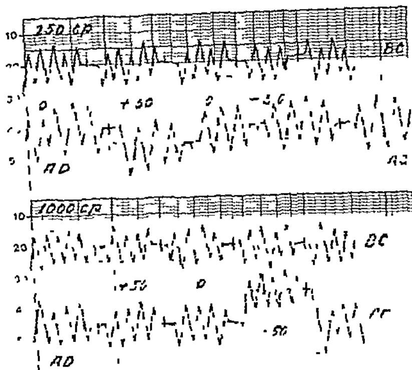


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The following case, referred by J. Swift Hanley, M.D., illustrates this point. A man aged 53 suffered from bilateral otosclerosis. He stated that self-inflation improved the hearing in his left ear. Fig. 5 demonstrates his Gellé test findings. In the upper portion, the reactions of the right ear are shown. It is obvious that BC suggests fixation of the stapes, while AC responds promptly to positive and negative meatal pressure, the latter being slightly more effective. This is a typically negative Gellé test, characteristic of otosclerosis.

In the lower section of Fig. 5 the Gellé test response of the left ear is shown

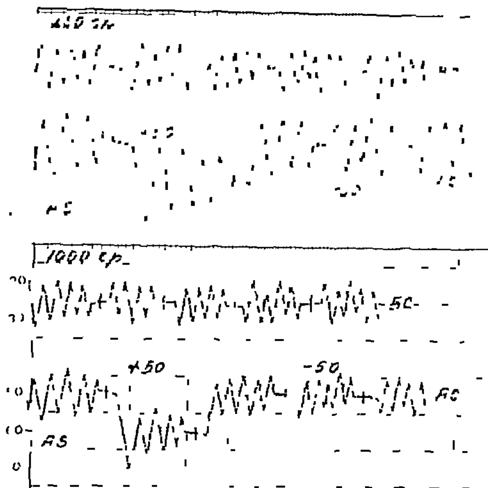


Fig. 4. Gellé test suggestive of otosclerosis. The BC curve does not shift with altered meatal pressure. Tested by AC, positive pressure shifts the threshold slightly, while negative pressure appears ineffective in this patient's left ear (comp. Fig. 3).

Again, the BC test reveals fixation of the stapes. In the second tracing the AC curve responds promptly to $+50$ cm H_2O by dropping sharply beyond the intensity range of the Békésy audiometer. In contrast, negative pressure of -50 cm H_2O improves the threshold by 3.4 db re the preceding 0 value or by 7.8 db re the subsequent 0 value. This is a test result suggestive of tubal obstruction, type two, of moderate amount.

Subsequently, the patient was instructed to inflate his tubes before the final test was recorded, shown in the lowermost tracing. At this point, positive pressure of $+50$ cm H_2O shifted his threshold again beyond the intensity range of the Békésy audiometer. By contrast, equivalent negative pressure did *not* improve the threshold anymore. Rather, it depressed the hearing level by about 3 db re the preceding and subsequent 0 values.

When the two AC tracings, recorded before and after self-inflation, are compared, it becomes obvious that the -50 cm H_2O value behaved in an *opposite manner* in these two tests. Before inflation, it improved the hearing level, but after inflation it depressed the threshold of hearing. In other words,

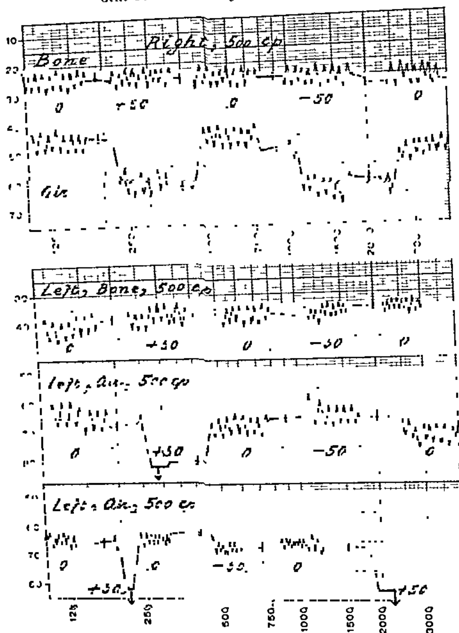


Fig. 5. Upper section: behavior of the right ear in bilateral otosclerosis. BC is not influenced by altered meatal pressure, while AC shows the normal response, negative pressure being more effective. Lower section: response of the left ear. Owing to sinistral tubal obstruction, negative pressure improves the AC threshold before self inflation. Afterwards, negative pressure results in a slightly impaired threshold, making the response more normal. BC continues to show stapedial fixation by absent pressure effects. The arrows at 50 cm pressure mean that the TTS extended beyond the maximal intensity range of the Békésy audiometer.

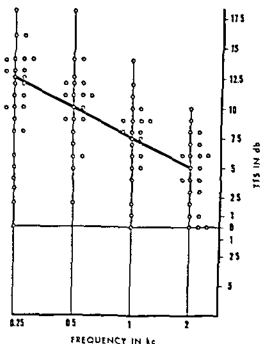


FIG 6 Effects of negative meatal pressure on AC in otosclerosis The most frequent responses are less great than in normal cases

after self-inflation the Gellé test returned to a more normal outcome of the AC result

Finally, when the rough average of 5–7 db hearing gain with negative pressure before inflation is added to the average of 3 db hearing loss with negative pressure after self-inflation, we arrive at a difference of about 8–10 db This value reflects the improvement in hearing acuity averred by such patients when they inflate their tubes In this manner, the Gellé test may confirm the co-existence of tubal obstruction as a complicating factor in otosclerosis This striking sensitivity of the Gellé test may aid in the differentiation among various types of conductive hearing loss

Predominant Results in Otosclerosis

Just as it is impossible to calculate a "mean" hearing loss in otosclerosis or any other type of hypoacusis, no average results of the audiometric Gellé test in otosclerosis can be evaluated It is, however, easy to demonstrate the trends observed in our first 50 patients studied in this manner

Fig 6 shows the responses to −50 cm H_2O negative pressure with AC at four different frequencies As is typical for normal ears, negative pressure is more effective than the positive equivalents, and the low tones are more affected than the higher frequencies These facts are portrayed by the slope of the curve through the predominant values In contrast to the average normal values, described in a previous paper (Arnold & Schindler, 1963*b*) the most frequently observed threshold shifts are less great than those encountered in normal subjects As can be seen, there are a number of otosclerotic

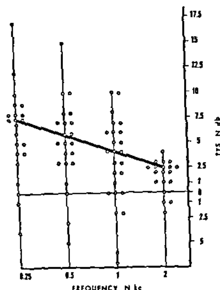


Fig. Effects of positive meatal pressure on AC in otosclerosis. Again the predominant readings of the audiometric Gellé test are reduced from the norm.

individuals who react with a negative Gellé test even with AC, that is, they show no or little TTS in response to altered meatal air pressure. It is established that variations of audiometric readings within 5 db may fall within the limits of error.

In Fig. 7 the effects of +50 cm H_2O positive pressure on AC are shown. Comparison with the corresponding illustration in the second paper (Arnold & Schindler 1963*b*) reveals that the predominant TTS in otosclerotic patients is smaller than in normal persons. The readings below the zero line, that is, negative values of TTS to a lowered (better) threshold, may represent two possibilities. In case of a negligible threshold shift by a few db only, such readings may mean that there was no significant response or a negative Gellé test. Secondly, a slightly improved threshold, especially at the frequen-



Fig. 8. Effects of negative meatal pressure on BC in otosclerosis, showing absent response of the negative Gellé test, as is typical for this disease.

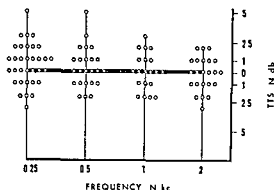


Fig. 9. Effect of positive meatal pressure on BC in otosclerotic patients again with negative Gellé test results.

cies around 2000 cps may indicate the normal behavior as described in our first paper (Arnold & Schindler 1963a).

Fig. 8 reflects the effects of —50 cm H_2O negative pressure on BC in cases of otosclerosis. It is immediately apparent that the Gellé test is ineffective or negative when administered by *BC in this disease*. A few patients did respond with a slight TTS up to 5 db. Such minimal degrees of response may indicate some residual mobility of the stapes. In view of the fact, however, that a rather similar number of patients showed improved hearing levels of 2–3 db, *these negligible threshold variations may fall within the margins of error.*

Fig. 9 illustrates the effects of +50 cm H_2O positive pressure on BC in otosclerosis. The majority of patients failed to respond to this meatal pressure application, giving a typical negative Gellé test reaction. Compared with the preceding Fig. 8, the scatterings are even smaller, lying between ±2.5 db. It would thus appear that the majority of these patients had a rather fixed stapes.

CONCLUSION

Preliminary experience with the audiometric Gellé test in 50 cases of otosclerosis revealed several interesting facts. To begin with, it confirmed the observations made by previous authors as described in our first paper (Arnold & Schindler 1963a). In addition, it could be shown that the Gellé test performed with Békésy audiometry is a rather sensitive procedure, permitting the differentiation between otosclerosis and salpingitis.

Fig. 10 presents a schematic outline of typical test results. In the upper curve the normal (or positive) Gellé test result is shown, as described in the preceding paper (Arnold & Schindler 1963c). *Then three types of a negative* Gellé test are defined which seem to reflect the main possibilities of pathologic results in otosclerosis. Similar to salpingitis, there are numerous transitions between these chief types found in clinical practice.

Slight to moderate stapedial fixation appears to be reflected by abnormally small values of TTS. Even though the normal pattern is preserved, the amount of TTS is reduced both by AC and BC.

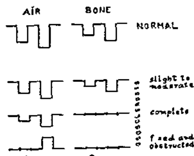


FIG 10 In contrast to the normal reaction otosclerosis appears to cause three types of an abnormal Gellé test reflecting the degrees of slight moderate and complete fixation as well as the combination with tubal obstruction

With complete fixation the pressure effect on AC is normal (Fig 1) or reduced (Fig 4) yet with preservation of the greater effectiveness of negative pressure In characteristic contrast BC is no longer affected by the pressure changes

Combination of stapedial fixation with tubal obstruction is suggested by an AC curve as in salpingitis while the BC curve fails to respond to pressure as is typical for ossicular fixation (Fig 5) Positive pressure becomes more or less ineffective both with AC and BC Characteristically the air bone gap may be momentarily closed in the AC curve during negative pressure application No such negative pressure effect is found by BC In summary the following formula seems to emerge

NORMAL Positive pressure is less effective than negative pressure AC is more affected than BC

OTOSCLEROSIS AC continues to be more affected than BC *Slight to moderate* normal pattern but with reduced shift *Complete* AC responses normal or reduced BC not influenced by pressure changes *Fixed and obstructed* positive pressure ineffective and negative pressure response inverted with AC while BC is not influenced

ACKNOWLEDGMENTS

Gratitude is expressed to Samuel Rosen, M D , for his permission to test some of his private patients before operation and to Mrs Yolan Schuller for her meticulous performance of the test procedure and the subsequent evaluation of the audiometric results

ZUSAMMENFASSUNG

Drei frühere Arbeiten über den audiometrischen Gellé Test waren den Problemen von Methode und Ausführung Definition der Normalwerte und den Befunden in Fällen von Tubenverschluss gewidmet Die vorliegende Studie befasst sich mit Beobachtungen an otosklerotischen Patienten

Als wesentlicher Befund liess sich bestätigen, dass Otosklerose die Hörschwellenverschiebung aufhebt, wenn der Effekt von verändertem Luftdruck im äusseren Gehörgang mit Knochenleitung gemessen wird. Im Gegensatz dazu verhält sich die Luftleitung eher wie in normalen Fällen, indem sie durch Druckänderungen verschiedengradig beeinflusst wird. Es kann aber auch sein, dass Druckänderungen im Gehörgang die Luftleitung nicht verändern, was für vorgeschrittene Stapesfixation spricht.

Wenn man den Ausfall des Gellé Versuches bei Luft- und Knochenleitung vergleicht, *lassen sich drei Haupttypen der pathologischen Befunde unterscheiden.* Sie scheinen die folgenden Schalleitungsstörungen anzudeuten: leichte bis mässige Fixation der Knochenkette, völlige Immobilisierung sowie die Kombination von Stapesfixation mit Tubenverschluss.

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Division of Otolaryngology
University Medical Center
Jackson 6, Miss., USA

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NEW INSTRUMENT

USE OF INDUSTRIAL TELEVISION CAMERA IN MICROSURGERY

Tokuro Suzuki
Matsumoto, Japan

From the Department of Otolaryngology, Shinshu University, Matsumoto

Television has proved a most valuable tool for demonstrating surgical operations in lecture rooms or other distant places. Color television system which is specially designed for medical use and is equipped with a large screen projector has already appeared on the market. It is indisputable that the reproduction of the actual color of the operating field is most essential for demonstrating operations through television. However, the initial installation and the maintenance of the medical color television system are much too expensive for routine clinical use. Furthermore, the color television camera is still too large and heavy to be mounted on an operation microscope.

Since the industrial television (ITV) camera of miniature type is now easily available at a moderate cost, one such ITV camera (HV 23CB, Shiba Electric Co. Ltd. Tokyo, Japan) has been mounted on the Zeiss operation microscope. It weighs only 2.3 kg and is fixed on the microscope with a specially devised supporter shown in the Figure. The lens of the ITV camera (F 1.4 25 mm) is brought into direct contact with the ocular of a side tube

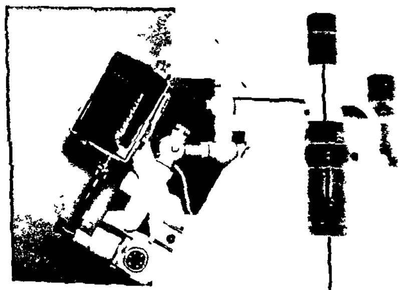


Fig. 1

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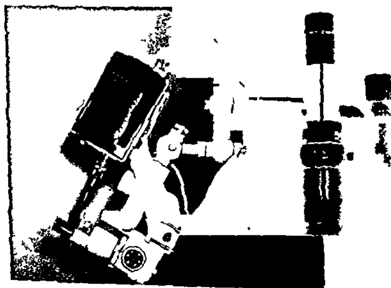


Fig. 1

for a second observer of the microscope. Neither an optical adaptor nor additional light is necessary to use the camera through the side tube of the microscope.

A well known bad feature of the side tube of the Zeiss microscope is that the image appears inverted as in a mirror, which disturbs considerably the orientation of the operating field by the second observer. This inverted image of the side tube can be corrected electrically by inverting the direction of the vertical electromagnetic deflection given to the vidicon tube in the ITV camera.

Of course, the image reproduced by this type of TV camera is not thought satisfactory for demonstrating delicate microsurgical procedures in full detail. Yet the author believes that the small size, easy handling and low cost of the equipment will cover this disadvantage.

Department of Otolaryngology, Faculty of Medicine, Shinshu University, Matsumoto, Japan

THE EFFECTS OF CUPULAR REMOVAL ON THE ACTIVITY OF AMPULLARY STRUCTURES IN THE PIGEON

GOSTA F. DOHLMAN[1] and ROBERT I. BOORD[2]

From the Laboratory of Neuroanatomical Sciences, National Institute of Neurological Diseases and Blindness, National Institutes of Health, U.S. Public Health Service, Department of Health, Education and Welfare, Bethesda, Maryland, U.S.A.

The effects of experimental removal of the pigeon cupula ampullaris were studied. It could be shown that the hairs of the sensory cells generally remain intact after this operation, suggesting that they are not fixed to the structures of the cupular substance. The cells of the transitional epithelium on the slopes of the crista showed an intense secretory activity as a result of the operation. The secretion appeared in the sections as eosinophilic globules. These globules were found in all parts of the endolymphatic space shortly after the operation, but were removed by the stream of secreted endolymph, except in the region of the sensory area where they were trapped by the hairs.

At a later postoperative period the globules in between the hairs are believed to be lifted beyond the tips of the hairs, thereby forming a new subcupular space. It is suggested that this could be the result of a histologically invisible secretion from the supporting cells of the sensory areas.

INTRODUCTION

The presence of globules or granules of eosinophilic substance commonly observed in the subcupular space at the surface of the hair cells of the cristae ampullares has never been accounted for and various interpretations have been assigned to them (Kaiser 1891, Kolmer 1911, Vilstrup 1950, Wersall 1956, Savin 1960). Furthermore, the relationship of these formations to cupular structure and their functional significance in the vestibular mechanism, if any, is obscure. There is some evidence, however, to indicate that they might play a role in the histogenesis of the cupula (Vilstrup 1950) and may be responsible for the regeneration of cupular substance following removal or injury. Werner (1933), for example, reports that the otolithic membranes can be reconstituted following their removal by centrifugation, but attributes this regeneration to the activity of the hairs of the sensory cells.

The purpose of this investigation, therefore, is to remove the cupulae in

[1] Present address: University of Toronto, Banting Institute, Toronto, Canada.
[2] Present address: University of Delaware, Newark, Del., U.S.A.

for a second observer of the microscope Neither an optical adaptor nor additional light is necessary to use the camera through the side tube of the microscope

A well known bad feature of the side tube of the Zeiss microscope is that the image appears inverted as in a mirror, which disturbs considerably the orientation of the operating field by the second observer This inverted image of the side tube can be corrected electrically by inverting the direction of the vertical electromagnetic deflection given to the vidicon tube in the ITV camera

Of course, the image reproduced by this type of TV camera is not thought satisfactory for demonstrating delicate microsurgical procedures in full detail Yet, the author believes that the small size, easy handling and low cost of the equipment will cover this disadvantage

Department of Otolaryngology Faculty of Medicine Shinshu University Matsumoto Japan

Kodak autoradiographic stripping film AR 10 The film was developed in order to show the distribution of sulphur compounds after an exposure period of 30 days

RESULTS

Thirty minutes following removal of the cupulae the subcupular zone has lost its integrity and the sensory hairs project into the endolymphatic space without a definite orientation (Fig 1) A few eosinophilic globules are deposited in between the sensory hairs but the epithelial areas in the ampullae present a normal appearance

A marked change occurs by 4 hours postoperatively Epithelial areas on the slopes of the crista and the epithelium of the eminentia cruciatum show intense secretory activity Eosinophilic globules are extruded from these secretory cells and frequently parts of or even entire cells appear to be expelled into the endolymphatic spaces (Fig 2) At this time the hairs of the sensory cells project upright into the lumen of the ampulla Many globules are deposited on their surface but may appear also between them and on the surface of the sensory epithelium

Two days following removal of the cupula the subcupular zone appears as a discrete entity (Fig 3) There is a further deposition of globules which now appear to be lifted off the surface of the sensory epithelium resulting in the reconstitution of the subcupular space and the sensory hairs have a more regular orientation The transitional epithelium remains intensely active (*Fig 4*) For the most part the secretory globules have become more compact *over the sensory* epithelium but more globules are also found in other areas throughout the ampulla as well as in the ductus and saccus endolymphaticus

Throughout the remainder of the postoperative period studied *up to 5* weeks the secretory globules progressively decrease in quantity in other areas of the labyrinth and become more restricted to a *position* over the sensory epithelium This corresponds to a decrease in the activity of the secretory epithelium which by the end of five weeks has returned to a near normal appearance and to a removal of the *globules through the* ductus and saccus endolymphaticus The subcupular zone remains discrete

Thus it is apparent that globules produced by the secretory epithelium in response to the irritation caused by *removal of the* cupula are removed from the ampulla by the stream of *secreted endolymph* except for the region of the hair cells where they are caught by *the hairs* Formations resembling these secretory globules are constantly seen in the ductus and saccus endolymphaticus *indicating that many* are removed by this route (Fig 5)

To study the fate of these *globules further* autoradiographic material proved of value At four days postoperatively and four hours after the intramuscular injection of S^{35} *most of the* epithelial areas in the ampullae exhibited some degree of radioactivity As was previously shown by Dohlman & Ormerod (1960) the sensory epithelium of the crista showed slight activity the transitional epithelium was moderately active whereas the secretory cells

the pigeon and report observations on the activity of ampullary structures as a result of this experimental interference, with special regard to the behavior of these eosinophilic globules.

MATERIALS AND METHODS

Adult healthy pigeons were used in all experiments. They were first given intramuscular injections of nembutal (approximately 20 mg/kg of body weight) followed by periodic etherization during the operation as necessary. The bony horizontal and posterior vertical semicircular canals and their ampullae on both sides were exposed by scraping away the muscle and spongy bone from a lateral approach. A small window was then made in the upper wall of the horizontal and the anterior wall of the posterior vertical ampullae with a sharp No. 11 scalpel blade, thus exposing the membranous ampullae. The ampullary walls were caused to collapse by sucking out the perilymph by vacuum using a small diameter pipette (approx. 30–50 μ). A small slit was then carefully cut in each ampulla and a little endolymph extracted. Presumably the collapse of the ampullary walls resulted in the detachment of the cupulae from the cristae which were then removed by gentle suction. Following the operation, the bony flaps were replaced on the ampullary walls and the incisions closed with surgical silk.

All pigeons survived the operations. The success of cupular removal was verified by blindfolding the animals and subjecting them to rotational tests. Animals were found to lose their reactions to rotational stimuli in the planes of the canals in which the cupulae had been removed.

At intervals of 30 minutes, 4 hours, 2 days, 3, 4 and 5 weeks following operations the animals were anesthetized and perfused after the method of Koenig, Groat & Windle (1945). The calvarium was removed and the heads further fixed and hardened by immersion in 10 % neutral formalin or in Heidenhain Susa fixative for 3 to 5 days. Two animals, which were allowed to survive for periods of 6 to 8 weeks were fixed according to Wittmaack's method. Following fixation, the heads were bisected in the mid saggital plane and those portions containing the inner ears, including the saccus endolymphaticus, were removed and processed by the parlodion technique. Sections were cut at 10–15 microns on the sliding microtome and stained with hematoxylin and eosin and the trichrome method of Rasmussen (1945). In general, serial sections were stained through the ampullary regions and every 10th section throughout the remainder of the labyrinth.

The effects of cupular removal on ampullary structures were studied in one animal by utilizing a radioactive isotope of sulphur as a tracer. In this pigeon, the cupulae were removed from the anterior vertical and horizontal canals of one side leaving the unoperated side as a control. Four days following the operation and 4 hours prior to sacrifice this animal was injected intramuscularly with S^{35} (7 millicures per kilogram of body weight). Paraffin serial sections of the inner ears were prepared and the slides covered with


1
2
EG
S
3

of the planum semilunatum were at the peak of activity (Fig. 6). The globules showed less radioactivity than the secretory cells of the transitional epithelium. They could be seen with assurance in all parts of the labyrinth and further observed in the ductus as well as the saccus endolymphaticus. In the saccus endolymphaticus they appeared to be partially dissolved indicating that they are absorbed there. It was possible to distinguish between the cloud-like formations of endolymph and globular formations deposited in the saccus before and after the injection of S^{35}. The globules and endolymph which had reached the saccus before the introduction of labelled sulphur showed no radioactivity while those sedimentations which were deposited in the saccus following the injection of S^{35} showed marked activity.

In the 6 and 8 week postoperative animals perfused with Wittmaack's fixative, very few globules could be observed but since the hairs were standing erect we believe that the fixative employed did not result in globular forms of these secretory products and therefore were not visible. The secretory cells appeared not unlike those seen in normal preparations.

DISCUSSION

Discrete spherical formations have been observed by numerous investigators between the sensory hairs in the subcupular space. These eosinophilic globules and granules have been variously interpreted with regard to both their structure and origin. Kaiser (1891) and Kolmer (1911) regarded them as postmortem artifacts. Vilstrup (1950), in the cod and shark, believed these cell-like structures to be products of the hair cells and sustentacular cells which gave rise to the cupula during histogenesis of the crista. Savin (1960) could not verify their origin from the epithelial cells of the crista in the chick but was able to demonstrate granular bodies which stain lightly with eosin among the sensory hairs. In the light and electron microscopic studies of Wersäll (1956) spherical bodies were also observed in the subcupular space in the guinea pig. This author believed them to be products of the sensory cells and not of the supporting cells as he previously reported (Wersäll 1954).

In normal well fixed preparations these globules are confined exclusively to the subcupular space between the sensory hairs and the base of the cupula.

Fig. 1. Crista ampullaris of the horizontal semicircular canal approximately one half hour following removal of the cupula. The subcupular zone is not apparent and the hairs project into the lumen of the ampulla in a haphazard manner. *Osmium fixation, phase contrast.* ×600.

Fig. 3. Sensory epithelium of the crista of the posterior semicircular canal [illegible] hours following cupular removal. Eosinophilic globules *(EG)* have been lifted off the surface of the hair cells resulting in the appearance *of a subcupular zone (SZ)* and the hairs project upright into the endolymphatic space of the ampulla. H & E stain. ×160.


EG
4
5
Secr. Ep
Sens. Ep
6

In the present experimental material, however, similarly stained globules occur in abundance throughout the endolymphatic space. It is unlikely that they are breakdown products of the detached cupula because no globular formations are observed within this structure. Therefore, it seems most likely that these globules represent secretory products of the transitional epithelium and that the increased secretory activity results from the traumatizing effect of removal of the cupula.

While it is difficult to confine the origin of these secretory globules exclusively to a definite group of cells, the great increase in activity indicates that they arise for the most part from the epithelial cells on the slopes of the cristae, termed the transitional epithelium by Kolmer (1911). Little attention as to their secretory function has been given these cells (von Fieandt & Savén, 1936) but the results of this experiment suggest that the secretory products may have a different composition and function than the secretions from the planum semilunatum. There is no evidence that the globules have their origin in the epithelium of the planum semilunatum since the secretions from this area can be observed to assume cloudlike formations after fixation and have been shown by Dohlman & Ormerod (1960) to penetrate cupular structures. Furthermore, the globules seem to exhibit less radioactivity four hours following the injection of S^{35}.

It is virtually impossible to determine, by routine histological methods, the mechanism by which these globules are deposited on the surface of the crista and then elevated to reconstitute the subcupular space. It is logical to assume that a secretory force exerted from beneath by the cells of the crista epithelium could be responsible. If this be true, a secretion from the crista epithelium, most probably from the supporting cells, must be different from the secretions which give rise to the globular formations.

These deductions therefore would infer that the subcupular space is maintained through secretions from three different sources. First, would be the mucopolysaccharide secreting cells of the planum semilunatum which embrace the side parts of the cupulae and pour their secretions directly into the open canalicular meshwork of the cupular substance. By means of autoradiography, it has been previously shown that this secretion pene-

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Fig. 4. Transitional epithelium (left) and the sensory epithelium (right) of the anterior semicircular canal two days following cupular removal. The secretory cells (arrow) of the transitional epithelium show intense activity and eosinophilic globules (E.G.) are deposited over the hairs of the sensory cells. A subcupular space is present. H. & E. stain. × 110.

Fig. 5. Eosinophilic globules in the saccus endolymphaticus three weeks following removal of the cupula. Formations as shown here are not present in preparations from normal animals. H. & E. stain. × 400.

Fig. 6. Radioautograph of portions of the secretory (Secr. E.p.) (planus semilunatum) and sensory (Sens. E.p.) epithelia from the ampulla of the posterior semicircular canal four days following removal of the cupula and four hours after the injection of S^{35}. Radioactivity is highest in the secretory epithelium. Slight activity is exhibited in the sensory epithelium and the coagulated endolymph and globules in the lumen of the ampulla. × 440.

the role played if any by the secretory globules in the reconstitution of the cupula

On the other hand it is untenable to assume that a structure like the cupula which snugly fits into the ampullary lumen would not be eroded as a result of its movements along the roof of the ampulla and replaced by some slowly growing action from the base So far, these experiments have not been able to prove or disprove the existence of such healing or reconstructing actions of the structures on the surface of the crista

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We wish to express our gratitude to Dr Grant L Rasmussen for the valuable discussions and the helpful assistance in the preparation of this paper

ZUSAMMENFASSUNG

Die Auswirkungen der experimentellen Beseitigung der Cupula ampullaris der Taube wurden untersucht Es wurde gezeigt, dass nach dieser Operation die Härchen der Sinneszellen im allgemeinen unbeschädigt bleiben, was andeutet, dass sie nicht in der Cupulasubstanz befestigt sind Die Zellen des Übergangsepithels an den Abhängen der Crista zeigten starke sekretorische Aktivität als Ergebnis der Operation Die Sekretion erschien in den mikroskopischen Präparaten als eosinophile Kugeln Diese Kugeln wurden kurz nach der Operation in allen Teilen des endolymphatischen Raumes gefunden aber wurden vom Strom der ausscheidenden Endolymphe beseitigt ausgenommen im Bereich der Sinneszone, wo sie von den Härchen festgehalten wurden

Bei einem späteren postoperativen Zeitpunkt wird angenommen, dass sich die Kugeln zwischen den Härchen über die Haarspitzen hinauf bewegen und damit einen neuen subcupularen Raum bilden Man nimmt an, dass dies das Ergebnis einer histologisch unsichtbaren Sekretion der Zellen der Sinneszone ist

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trates as far as the subcupular space and presumably as far as the cell surface (Dohlman & Ormerod 1960).

The second source of secretion envading the subcupular space originates from the transitional cell zone and forms eosinophilic globules in the region of the hairs of the sensory cells.

The third source is assumed to emanate from the surface of the supporting cells of the sensory area. The basis for this notion is that the subcupular space appears to be first reorganized and then lifted up from this region.

We are certainly aware of the fact that what has been described here as radioactive "clouds" from the secretion of planum semilunatum cells, "globules" from the transitional epithelium and the invisible secretion from the surface of the crista forming the subcupular space are "artifacts" in the strict sense of the word. The endolymph is coagulated by the fixing agents, the protein bound mucopolysaccharides sedimentate forming "clouds", are radioactive because they contain sulphur compounds.

Our line of reasoning is that the globules from the transitional epithelium acquire this special form and stain eosinophilic because they have a different origin and composition and there is no evidence that they should appear in the form of globules in the living labyrinth. The fact that very few of the globules are seen in tissues fixed with Wittmaack's solution while many are observed in an animal perfused with formalin tends to support this idea.

It is recognized that our method of approach does permit the determination of the route taken by the globular secretion in order to reach the subcupular space. In fixed and dehydrated material it is impossible to determine the exact region covered by the cupula. In some ears, which were embedded in polyvinyl alcohol without previous fixation, the cupula appeared to cover not only the sensory area but also parts of the transitional epithelium. If this were the case it would explain the fact that part of the secretion from these cells could pass into the subcupular space.

However, this does not explain why the globules, after ablation of the cupula, accumulate in the region of the hairs of the sensory cells. The way in which this secretion appears as globules suggests a higher viscosity here than elsewhere. Presumably this viscous secretion would be entrapped more easily by the hairs of the sensory cells than in other regions where the fluid from the secreting planum semilunatum can remove the globular secretion. Furthermore there is evidence indicating that this secretion is transported to remote regions.

Radioactive globules in experiments with labelled isotopes are found in abundance in the ductus and saccus endolymphaticus of the operated ears.

There is also a possibility that this secretion is attracted to the surface of the hairs because of their electrical charge but this cannot be proven until more is known about the chemical and electrical properties of this secretion.

No evidence of reformation of a cupula could be noted in these experiments of short postoperative periods and therefore nothing can be said about

SECRETORY EPITHELIAL LININGS IN THE AMPULLAE OF THE GUINEA PIG LABYRINTH

R. KIMURA[1], P. G. LUNDQUIST and J. WERSÄLL
Stockholm, Sweden

From King Gustaf V Research Institute (Head: Prof. G. Birke), Department of Oto-laryngology (Head: Prof. C. A. Hamberger), Karolinska Sjukhuset, and Department of Histology (Head: Prof. N. Å. Hillarp), Karolinska Institutet, Stockholm 60, Sweden

Three major epithelial linings of the ampulla were investigated with the electromicroscope with special reference to their morphological characteristics and it is attempted to correlate these with the possible function of this area. All these epithelia, the sensory supporting cells, planum semilunatum and dark cells demonstrate some features which are suggestive of secretory and perhaps reabsorptive processes. However, further investigations will clearly be required before these two functions can be correlated more specifically to the precise cell areas in which they occur.

INTRODUCTION

The electron microscopic structure of sensory cells and nerve endings in the cristae ampullares are well documented (Wersäll 1954, 1956, 1961; Engström & Wersäll 1958; Engström 1960; Bairati 1960; Trujillo Cenoz 1961; Flock & Wersäll 1962). However, information concerning other structures of physiological importance in this area is rather meagre.

It is possible to identify three different types of non-sensory epithelial cells in the ampulla. These are of particular interest and often regarded as having a secretory function.

The epithelium of the rat's planum semilunatum has been described as a filter of cochlear fluid thereby producing endolymph (Bairati & Iurato 1960).

Similar findings have been described in the epithelium of the non-sensory area of the utricle (Smith 1956).

Thirdly, glandular structures in the epithelium of the base of the utricle have been described from routine histological studies (Borghesan 1961) but not electromicroscopically.

Supporting cells are also present and their numerous large granules are suggestive also of some secretory function (Wersäll 1956).

In the present investigation we intend to describe those three zones in detail starting from the top of the cristae and continuing from there in an orderly manner with special emphasis on the morphological characteristics pertaining to secretion and absorption of labyrinthine fluid.

[1] Harvard Medical School and Massachusetts Eye and Ear Infirmary, Boston, U.S.A.

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Fig. 1. Low magnification of the sensory supporting cells located at the outer margin of the sensory cell area (S). They contain numerous granules, comparatively few mitochondria and sometimes a large dark oval mass. At the basal portion of the supporting cells the nerve fibers and their enlargements (N) are demonstrated. Osmium tetroxide. ×4000.

MATERIAL AND METHOD

One albino and nine non-albino guinea pigs were killed by decapitation. The entire vestibular structure was fixed in 1 % osmium tetroxide in less than four minutes after opening the round window, lifting stapes and widening the cistern of the vestibule. The utricle and semicircular canals were opened adjacent to the ampulla to facilitate the penetration of the fixative. The ampullae were dissected out in 70 % alcohol, imbedded in Epon, cut with a LKB ultrotome and stained with uranyl acetate. All superior, horizontal and posterior ampullae were examined. Some ampullae were cut at three different angles: vertically in the long axis of the utricle and canal openings, vertically in the long axis of the cristae and horizontally starting from the top extending to the bottom of the ampullae. The thin sections were photographed with Siemens Elmiscope 1 with an initial magnification ranging from [illegible]00 to 20 000.

FINDINGS

1. *Sensory supporting cells*

Differing from Deiter's cells in the cochlea, the apical surface of the sensory supporting cells reached to the same fluid level as the sensory cells. The sur-



Fig. 2. The apical zone of the sensory supporting cell shows many large granules and the Golgi network. The insert reveals a centriole on the fluid surface of the supporting cell located among the sensory cells. Osmium tetroxide. ×22 500. Insert ×30 000.

face was smooth except between the sensory cells where microvilli were occasionally seen. The shape of the supporting cells varied greatly. Their nuclei were oval, contained large nucleoli and were located at the extreme basal portion of the epithelium. When the peripheral supporting cells were examined in the region of the base and side walls of the ampulla they became columnar to cuboidal (Fig. 1) and formed a band of several rows around the neurosensory epithelium. One of the most striking features of these supporting cells was that they contained numerous large oval and oblong shaped granules throughout their cytoplasm, somewhat more concentrated at the apical zone in those found among the sensory cells. These granules were sharply outlined by dark staining membranes and themselves contained numerous minute granules. Another type of larger dense granular formation was occasionally seen in the apical zone. It was irregular in shape and the fine outer membrane appeared often to be discontinuous but this may well be artifact.

A centriole was located at the apical surface, often in a vertical position. Whether they were present in all supporting cells or specifically orientated as those of the sensory cells has not been determined. The Golgi apparatus was usually located in the apical portion and mitochondria were scattered

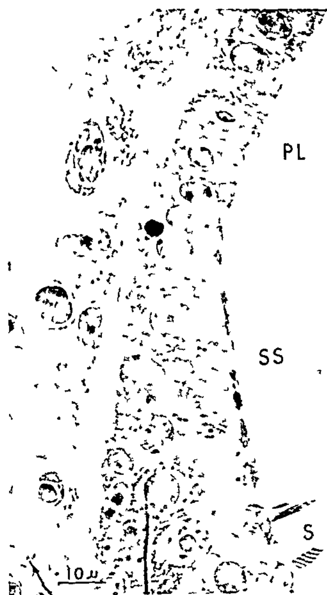


Fig. 3. Low magnification of the side wall of the ampullae sectioned at the top of the cristae vertically in the right angle to the axis of the utricular and canal openings. It demonstrates a gradual transition from sensory cells (S) to the sensory supporting cells (SS) and to the planum semilunatum (PL). A wide zone of fibrous layer and a few capillaries are also shown below the epithelial lining. Osmium tetroxide. × 1100.

and few (Fig. 2). Occasionally a large dark oval mass was found in the lower part of the supporting cell. There was no elaborate plasma folding at the basal part of the epithelium.

The nerve fibers were not limited to the sensory cell area but extended among the sensory supporting cells at the periphery. They were often located in deep groves on the cell surface reaching close to the nuclei and their bulbous enlargement appeared as if they might be nerve endings (Fig. 1).

2. *Planum semilunatum*

As the crista was followed towards the side wall at the right angle to the axis of the utricular and canal openings, the number of sensory cells became less

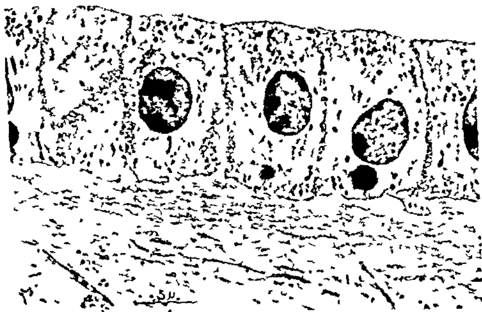


Fig. 4. The planum semilunatum shows a smooth apical surface and numerous finger like projections between the cell borders. Most of the dark formations at *the apical margin* are large granules (see Fig. 6). The Golgi structures are prominent, and the number of mitochondria is moderate without any localization. Below the basement membrane there is a *zone of fine fibrous* layer which is composed and interwoven with diagonally running fibers. Osmium tetroxide. × 3400.

being replaced first by columnar supporting cells *and then* by the epithelial lining of the planum semilunatum (Fig. 3). *Thus there* was a gradual transition *from* the supporting cells to planum cells. At the proximity of the cristae *the* planum epithelium was columnar (Fig. 4) but became gradually cuboidal loosing the *reticular lamina* as it shifted towards the utricle canal and dome of the *ampulla* (Fig. 3). The shape of the planum *semilunatum looked* like a partially eclipsed moon and the *epithelial lining* was arranged in the slight concavity. It did not extend to the *midline at the bottom* of the ampulla.

The *cell surface apposed to the endolymph* was very *smooth* (Fig. 4) while the plasma membrane between the *adjacent* cells showed numerous long finger like projections, sometimes filling *large parts* of the cell or cutting across the cytoplasm in a narrow *band*. The basal portion of the epithelium also demonstrated finger like *processes*, but to a lesser degree, and was lined by an apparently continuous *basement* membrane (Fig. 5).

The nucleus was oval and located randomly. *Light and* dark granules were seen, the most conspicuous being large dark ones present in varying *numbers* particularly in the vicinity of the cristae *and* decreased gradually towards the periphery. Vacuoles of varying *shape and* size were also seen. At the basal and middle portions of the epithelium there were found very large dark oval
If the size of the nucleus



FIG 5 The basal portion of the planum semilunatum demonstrates extremely numerous finger like projections within the cytoplasm and between the cells Sometimes such finger like cytoplasmic processes occupy almost the entire cytoplasmic area Osmium tetroxide × 17 000

The Golgi network was prominent close to the surface, and centrioles were occasionally found between the Golgi structure and the apical cell border (Fig 6) Rod-shaped mitochondria were scattered but not numerous

Immediately below the basement membrane was found a wide zone of dense, fine fibrous structures which were intermixed from below with diagonally running fibers The capillaries did not show any special modification in their endothelium but were located fairly close to this fine fibrous zone

Nerve fibers were not found in the epithelial linings of the planum semilunatum

3 *Dark cells and transitional epithelium*

As the crista of the guinea pig was followed towards the base in the axis of the utricular and canal openings, there was usually a slight epithelial elevation which indicated the end of the sensory and columnar supporting cells Then came a shallow *depression in which the transitional cells were* found The morphological characteristics of the transitional epithelium were fairly similar to those of the planum semilunatum (Fig 7) The transitional epithelium was mainly columnar, but at the high and low margins of the depression a few cells became cuboidal The columnar cells contained numer



FIG 6 The apical surface of the planum semilunatum shows large dark granules light granules and a centriole The centriole is usually located near the fluid surface but its direction of the long axis is not necessarily in a vertical position as shown here Osmium tetroxide ×26 000

ous dark granules and some light oval granules at the apical zone The cuboidal cells on the other hand showed more oval granules and some dark granules The finger like projections were numerous at the cell borders and even deep in the cytoplasm Their nuclei were located mainly at the basal part of the cell which showed more convexity towards the loose fine fibrous zone

There was normally a second epithelial elevation which indicated the end of the transitional epithelium and the beginning of a zone of dark cells at the base of the cristae (Fig 8) This zone of dark epithelial lining followed fairly closely the distribution of the pigment cell layers found in the ampulla They were not restricted to the basal area of the crista but rose up to form a high complete ring around the utricular opening and they were thus continuous with the similar epithelium of the non macular portion of the utricle This dark epithelium was also located in the canal side in form of a wide U band with its opening facing dorsally towards the canal discontinuous from the utricular side In the albino guinea pig visualization of these dark cells became difficult due to lack of pigment The dark cells were interspersed in the planum semilunatum thus it was possible to confuse them

The shape and size of the dark cells varied depending on their location (Fig 9) The dark cells were tall near to the crista with their loose basal processes extending far out into the connective tissue or even running below parallel to the transitional and planum epithelia for some distance Occasionally single isolated dark cells were found among these latter groups of epi

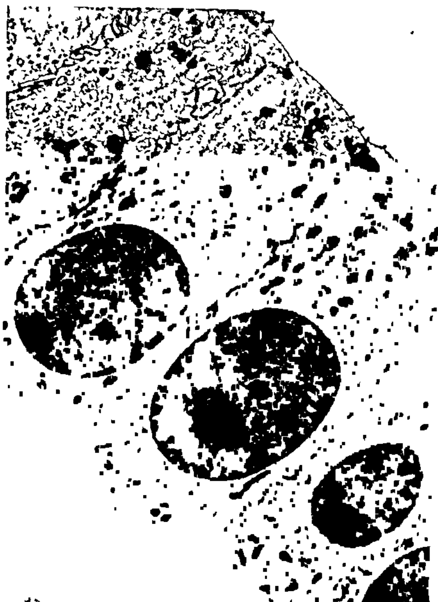


Fig. 7. The transitional epithelium demonstrates large dark granules, light granules, Golgi apparatus and many short membranous structures in the apical zone. The cell border reveals complicated cytoplasmatic interdigitations. The base of the epithelium is convex with a distinct basement membrane, and rests on a loose fine fibrous zone. Osmium tetroxide. × 7000.

thelia. At the more peripheral areas of the crista, these dark cells became first cuboidal, then squamous, resting on a comparatively smooth basement membrane. In general the cell surface on the apical side was smooth, even though they sometimes showed an irregular pitted appearance as if small openings were continuous with the vacuoles. The cell boundaries became difficult to determine at the middle and lower parts of the epithelium due to many complicated cytoplasmatic processes.

The nucleus was randomly located, but more often occupied the upper portion of the epithelium and had a great irregularity in shape. The dense apical zone contained numerous dark granular masses and vacuoles of vary-



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ing size Rode shaped m tochon lria and *many short* membran us processes l elonging t the endoplasmatic *reticulum were also seen* (*Fig 10*) *F* inger like invag nations were *in contact* with the apparently cont nuous basement meml rane (F g 11) The capillaries in the subepithelial zone did not show any special features *in* their endothelial wall

DISCUSSION

In the present study we have investigated the three major epithelial linings of the ampulla which *are of part cular* importance for the understanding of the physiology of the vestibular fluid As far as we can see there are no gross



FIG 9 The dark cells at the proximity of the transitional epithelium are tall, changing gradually into cuboidal or squamous type in the peripheral zone The nuclei are irregular, and the cytoplasm contains complicated network of cytoplasmic processes basally Osmium tetroxide ×3600

ultrastructural differences in these epithelia of the superior, horizontal and posterior ampullae Neither are there distinguishing morphological characteristics to point out if they belong to the canal or utricular side, except the position of the Kinocilium

The presence of granules in the sensory supporting cells corroborated previous studies (Wersall, 1956) Similar granules were also seen in the cells of the planum and transitional epithelial zone, but they were notably absent in the dark cells of the ampulla Their position in the cell was usually near the fluid surface adjacent to the Golgi apparatus and in some areas they appeared to release their contents, a fact which reinforced Wersall's theory that they are secretory in nature

The predominance of these granules in the area of the cupular substances may suggest that they contain some substance which would contribute to the formation of this gelatinous cupular covering



FIG 10 The apical and middle parts of the *dark cells* in a diagonal section reveal a dense cyto plasm containing numerous large dark *granules* *vacuoles* of varying size short membranous structures and many mitochondria Osmium tetroxide ×8400

From experiments with Streptomycin intoxication in the crista ampullaris it has also been suggested (Wersall & Hawkins, 1961) that the supporting cells might be involved in the secretion of toxic drugs into the endolymphatic space

The ultrastructure of the planum semilunatum and the transitional epithelium are similar in many respects, and therefore their functional roles at least in parts may be the same The structure of the planum semilunatum in the rat (Bairati & Iurato 1960) differs considerably with that of the guinea pig in the present study, even though checked by cutting in many different angles Whether this be due to different definitions of what constitutes the planum semilunatum or to different morphological characteristics in different species is not certain

It has generally been regarded that the planum semilunatum is concerned in



FIG. 11. The basal portion of the dark cell shows the long cytoplasmic extensions with the bulbous enlargement containing mitochondria. The cytoplasmic processes are limited at the basement membrane. Osmium tetroxide. × 20 000.

some form of secretory activities (von Fieandt & Saxén 1936, Dohlman, Ormerod & McLay 1960, Bairati & Iurato 1960, Borghesan 1961, Anggård personal communication). The nature of the secretion was investigated with radioactive sulphur injections into pigeons (Dohlman & Anggård) and found to be a sulpho-muco-polysaccharide. The planum epithelia has been described as being concerned with the endolymph production of the vestibular area by a filtration process (Bairati & Iurato 1960).

The present investigations show that the planum epithelium possesses some of the characteristics (e.g. two different types of granules, finger-like projections and numerous vesicles) which have been related to filtration and secretion in other areas such as the kidney (Rhodin 1958), pancreas (Ekholm *et al.* 1962), ciliary body and choroid plexus (Pease 1956) and stria vascularis (Engström, Sjöstrand & Spoendlin 1955, Smith 1957).

The evidence however although being most suggestive cannot be regarded as conclusive

The ultrastructure of the stria vascularis which is known to produce endolymph in the cochlea is quite different from that of the planum semilunatum or the transitional epithelium If therefore the planum is the major source of endolymph in the vestibular system as proposed then the morphological difference may imply a difference in the mode of secretion of specific substances in these two areas

The terminology The dark cells is used in the present description in referring to the special epithelial linings found on both sides of the crista (Kolmer, 1907 Iwata 1924) These dark cells form a continuous layer extending outwards into the utricular body, and are identical to those reported in the non sensory area of the utricle (Smith 1956) The structures of these cells may be regarded as indicative both of a resorptive and secretory function They show certain morphological similarities to those in the distal renal tubules (Rhodin 1958) and the striated duct cells of the parotid gland (Rutberg 1961) both of which are known to selectively reabsorb sodium The basal half of the epithelium is filled by numerous slender cytoplasmic processes and the apical zone with vacuoles dark granules and short endoplasmic tubuli The capillaries are not particularly numerous and fail to show the fenestrae in their endothelial wall as seen in the endolymphatic sac (Lundquist Kimura & Wersall 1964) or in the kidney Lying close to the basement membrane of the dark cells is an area of pigment cells which is of particular interest having been previously described in the ciliary body of the eye The latter is of course concerned with fluid transport, but it is not possible at this stage to be definite that those of the ear have a similar function

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ZUSAMMENFASSUNG

Drei hauptsächliche Epithele von der Amp

Alle diese Epithele die Stützzellen des Sinnenepithels Planum semilunatum und dunkle Zellen weisen einige Kennzeichen auf die sekretorische und vielleicht reabsorptive Prozesse andeuten Weitere Studien müssen aber offenbar ausgeführt werden, ehe diese zwei Funktionen in näherem Verhältnis zu den besonderen Zellenabschnitten, wo sie auftreten gesetzt werden können

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Department of Otolaryngology, Karolinska Sjukhuset, Stockholm 60, Sweden.

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PRINCIPLES FOR THE TREATMENT OF CHILDREN WITH RESPIRATORY DISTRESS

G. BECHMANN and I. I. SANDBERG
Gentofte, Denmark

From the Department of Otolaryngology (Head: Prof. N. Riskær) and the Department of Anaesthetics (Head: Dr. S. H. Johansen), Copenhagen County Hospital, Gentofte

Taking as starting point the case history of a two-month-old boy, the therapeutic possibilities which are available for the treatment of respiratory depression of various aetiology in children are described.

If the conservative regime comprising treatment with medicaments, oxygen, alevaire, fluid and pulmonary physiotherapy is insufficient, intubation with thorough aspiration of secretions and possibly delivery of air containing a high percentage of oxygen is recommended.

In cases of longer duration it is recommended that tracheotomy, possibly supplemented with intermittent positive pressure respiration, either manual or mechanical, be carried out. The advantages and drawbacks of the treatment are mentioned. Intermittent positive pressure ventilation is considered to be a "survival therapy" by means of which time can be gained to make it possible to fight the underlying disease with more specific therapy.

Severe respiratory distress, which in children is most frequently caused by acute infectious disease, has hitherto had a high mortality rate. This has been reduced in more recent years thanks to the increasing knowledge of antibiotics, fluid-electrolyte therapy, and of the problems involved in tracheotomy, the moistening of the inspiratory air, pulmonary physiotherapy, etc.

However, cases still occur which do not respond satisfactorily to the therapeutic methods mentioned above. In such situations ventilation therapy can be directly lifesaving, as is well illustrated by the following case history.

Case History

A two-month-old, previously healthy, boy was admitted from a children's home having had a cold for a few days. Shortly before admission there had been an acute deterioration in his condition, with circulatory collapse and respiratory arrest which was treated on the spot by artificial respiration, after which his condition improved.

In the Department of Paediatrics bilateral pneumonia was diagnosed and this was confirmed by X-ray. Treatment with sulphonamide drugs and Terramycin was immediately instituted and the child was placed in an oxygen tent. His condition, however, continued to deteriorate and he became

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Department of Otolaryngology, Karolinska Sjukhuset, Stockholm 60, Sweden

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changed daily later this was carried out at weekly intervals Daily pulmonary physiotherapy was given and secretions were aspirated as required Throughout the entire period it was possible to maintain the child s temperature at normal levels merely by regulating his coverings Chemotherapy was completely withdrawn after the 14th day

His general condition was apart from during the first critical days strikingly good all the time Thus it was for example possible to avoid loss of weight thanks to the fact that throughout the entire illness the child was able to take milk mixtures in the amounts and strengths appropriate to his age at first the feeds were given by stomach tube later by bottle It was therefore at no time necessary to give parental fluids

From the 14th day the child was completely well apart from the fact that attempts to remove the tracheostomy cannula met with considerable difficulties

On the 12th day the cannula was changed to one with a side hole and the tracheostomy was occluded daily with a cork for increasingly longer periods On the 29th day an attempt was made to remove the tracheostomy cannula but about 12 hours later re tracheostomy had to be performed due to the recurrence of respiratory insufficiency It was not possible to remove the cannula until 10 months after the original tracheotomy

The general condition of the child is still completely satisfactory one year later He is developing normally both mentally and physically

Review of Possible Modes of Treatment

The cause of the respiratory insufficiency in children is in by far the majority of cases acute infection of the respiratory tract A smaller proportion of cases are due to prematurity debility congenital malformations diseases of the nervous system and trauma The therapeutic possibilities are in general the same for all the various groups Those children whose symptoms do not respond to the usual treatment consisting of chemotherapy oxygen alevaire tent cortisone postural therapy pulmonary physiotherapy sedation and fluid electrolyte therapy will as treatment is gradually intensified sooner or later be referred in increasing numbers to the staff of the E N T department for diagnosis and therapy We will therefore give an outline of what apparatus and what possible modes of therapy are additionally available

Intubation

If the child has accumulation of secretions and an inadequate cough it can be of great benefit to aspirate via an oro tracheal tube or bronchoscope If necessary this procedure can be repeated several times daily

In more severe cases it can be advantageous to keep the tracheal tube in place for a period of hours or perhaps for up to two days In some centres it is considered preferable to retain the orotracheal tube for periods of up to several weeks if necessary (Armstrong 1958) The danger of this procedure

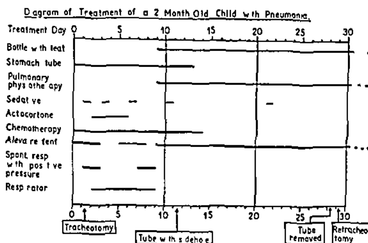


Fig. 1. Diagram illustrating the treatment during the first month.

increasingly dyspnoeic, with cyanosis and inspiratory retractions. Intubation and aspiration of secretions from the trachea did not give any relief, and it was therefore decided that tracheotomy should be performed. The operation was carried out in Fluothane anaesthesia, with insertion of the tracheostomy cannula through the third tracheal cartilage. The operation proceeded without complications.

After operation it became apparent that despite repeated aspiration of secretion from the trachea, the child continued to suffer from difficulty with breathing, and he was restless due to hypoxia. An attempt to calm the child with phenothiazine, in order to reduce his oxygen requirements, was unsuccessful. An attempt was therefore made to allow the child to breathe from and into a respiratory bag which contained oxygen at a pressure slightly above atmospheric. By this means the respiration was improved to such an extent that after 6 hours the child was able to manage in an oxygen alevaire tent.

Because of the excessive amount of secretion it was necessary to aspirate repeatedly through the tracheostomy, each aspiration being preceded by the instillation of isotonic sodium bicarbonate. Twenty four hours later, however, the child again became atonic and pale with prolonged expiration and inspiratory retractions. Actocortone therapy and manual intermittent positive pressure ventilation were therefore commenced.

Although he once again improved, it now became clear that it would be necessary to give artificial respiration for a longer period, and it was therefore decided that the child should be treated in a mechanical respirator. Details of the further therapy are given in Fig. 1.

During the next 3 days the child was ventilated exclusively by respirator at first with pure oxygen, and later with a gradually decreasing percentage of oxygen until he could manage with atmospheric air alone. The respirator therapy was thereafter gradually reduced over the course of 3 days, being alternated with periods of spontaneous respiration either from a bag, or in the oxygen alevaire tent. In the beginning the tracheostomy cannula was

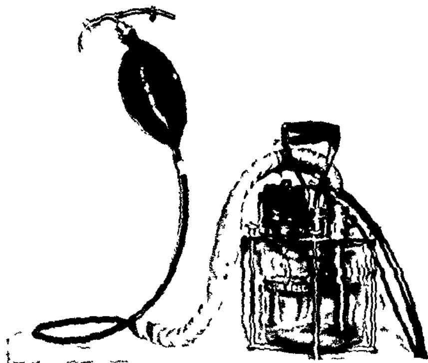


Fig 3 Thermostatically controlled humidifying aggregate and transfer bag with *Ayre's T piece*

for the fixation of a heat humidity exchanger the so called artificial nose The artificial nose is very useful in children over the age of one year In children younger than this we have found it too heavy and too difficult to keep in the proper position we still prefer to place these children in an oxygen alevaire tent or else to connect the cannula directly to a special aggregate for humidifying the inspiratory air

The collar is extremely well adapted for connecting the tracheal cannula to the ventilation apparatus without the already small lumen being further diminished and the resistance thereby increased

Tracheotomy will in by far the majority of cases ensure adequate respiration for the child provided that it is managed very carefully with cleaning and change of the tube together with aspiration of secretions and humidifying of the inspired air

In these patients it is of utmost importance to keep the oxygen requirements low by maintaining the body temperature at approximately normal levels and also to keep the child quiet with the aid of small doses of sedatives

Oxygen under positive pressure

If the respiratory insufficiency persists after tracheotomy despite the use of oxygen (for example because of impairment of pulmonary diffusion) it

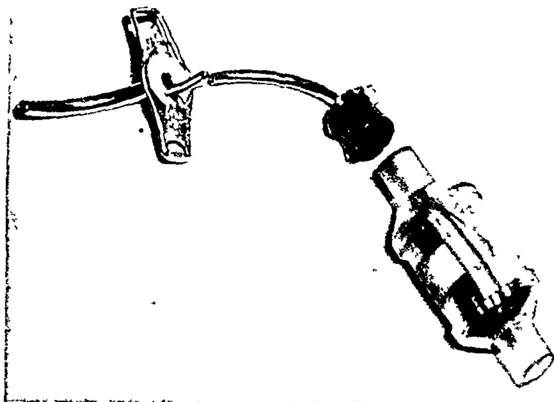


Fig. 2. The tracheal cannula (left), the inner cannula with collar (centre) and the heat-humidity exchanger called "the artificial nose" (right).

is the occurrence of irritative oedema of the larynx, which may impede the changing of the tube and a later tracheotomy, if it be indicated.

The advantages of prolonged orotracheal intubation are: The elimination of the danger of mechanical obstruction such as may occur, for example, if the tongue falls back, if the nares become blocked, or if secretions accumulate in the upper respiratory tract. The dead space is considerably reduced. There is easy access for frequent and thorough aspiration. If an atelectasis has developed behind the accumulated secretions, it may be possible, by means of positive pressure ventilation, to reinflate the atelectic area.

After a short time this treatment will in many cases have relieved the child to such an extent that it has survived the critical period, and can manage alone after extubation.

Tracheotomy

If it is estimated that the respiratory insufficiency will be of long duration, it is in our opinion necessary to undertake tracheotomy. In our experience this is carried out most easily and safely in general anaesthesia with orotracheal intubation.

The silver cannula with collar, described by Toremalm (1960*a*) is extremely useful, especially in small children (Fig. 2). The collar was originally designed

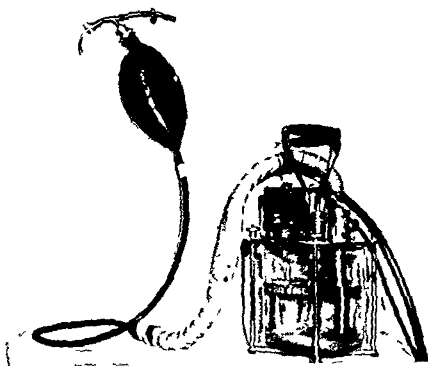


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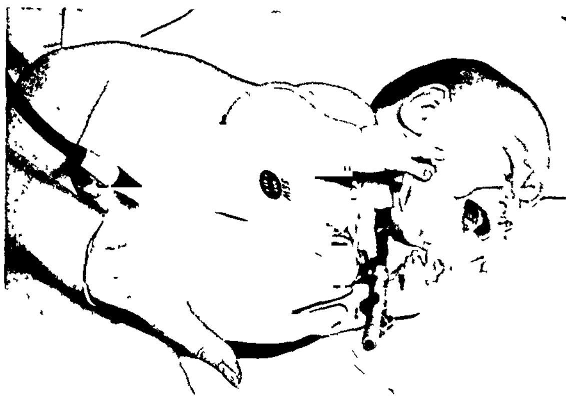


FIG. 4. The system in use. The transfer bag with T piece connected to the "artificial nose" which again is connected to the collar of the tracheal cannula.

is possible to offer the child oxygen in such a manner that the expiration takes place against a positive pressure of a few mm Hg.

For this purpose we use the system shown in Figs. 3 and 4. The oxygen is conducted through a thermostatically controlled humidifying aggregate to a transfer bag, and thereafter to a so called Ayre's T-piece (Ayre, 1937), one branch of which is a connector which fits the collar of the tracheal tube, whilst the other branch is fitted with a rubber tube which can be partially occluded by means of a screw clamp so that the constant flow creates a slight positive pressure in the bag.

It has been found from experience that expiration against this small pressure relieves a number of these patients to such an extent that the ventilation becomes sufficient.

Artificial respiration

If the above also proves insufficient, the last remaining possibility is the institution of artificial respiration. In its simplest form this is achieved by intermittent pressure on the bag in the system described above. In some cases as, for example, the child described in this paper, we have found it necessary to use considerable inspiratory pressure in order to overcome the resistance produced by stagnant secretions and oedema of the mucous membrane

The correct pressure to use can in practice be judged by observing the thoracic excursions and the colour of the skin Further information relating to the ventilatory status of the patient can be obtained by measuring oxygen saturation and carbon dioxide tension in the arterial blood

Manual respiration calls for specially trained personnel If it is to be continued for long periods practical problems will therefore arise Attempts have therefore been made for a number of years to devise reliable respirators Although some of these have reached high standards the mechanical respiration of children and especially of new born and premature infants still gives rise to technical and practical difficulties (Mushin *et al* 1962, Norlander, 1961)

Complications

The occurrence of complications of tracheotomy depends amongst other things upon the skill and experience of the surgical team and the ward staff From this point of view it is considered advantageous that the tracheotomies should be centralized in the hands of the otologists This is especially true when the patients are children in whom the technical difficulties are greatest

Toremalm (1960*b*) has published a material from the two years 1958 59 consisting of 25 children aged from 4 weeks to 10 years He found one case of mediastinal emphysema two of post operative pneumonia and two of crust formation In 13 of the patients i e one half the tube was removed within the first fortnight one patient developed a stenosis and the tube could first be removed after a year There were no cases of pneumothorax or atelectasis

There is a certain risk of damage to the lung tissue if it is necessary to use pressures in excess of approx 10 15 cm water which is the pressure used when children with normal lungs are ventilated

In this case there is no choice as the children concerned will succumb if it is not possible to convey to the lungs a sufficiently large amount of oxygen to maintain the normal oxygen supply to the tissues

The dangers associated with positive pressure ventilation are, however undoubtedly overestimated In all events there have been no fatal complications reported in the literature in publications coming from hospitals in which the treatment of these patients is centralized (Benson 1958)

ZUSAMMENFASSUNG

Mit der Krankengeschichte eines zweimonatigen Jungen als Ausgangspunkt werden die therapeutischen Möglichkeiten die Kindern mit Atmungsdepression von variierender Ätiologie zur Verfugung stehen, beschrieben

Falls ein konservatives Behandlungsschema mit Medikamenten Sauerstoff Alevaire, Zufuhr von Flussigkeit sowie Lungenphysiotherapie nicht genugt, empfiehlt sich eine Intubation mit gründlichem Aufsaugen des Sekrets und mit eventueller Zufuhr von Luft mit hohem Sauerstoffprozent

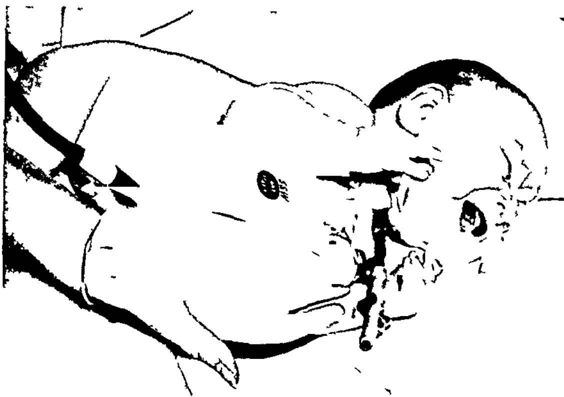


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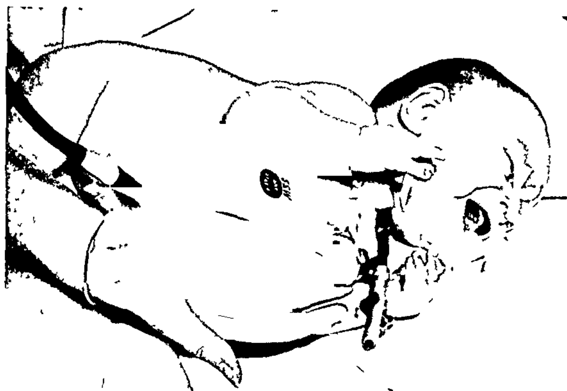


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VESTIBULAR REACTIVITY IN CASES OF CONGENITAL NYSTAGMUS AND BLINDNESS

B. FORSSMAN
Lund, Sweden

From the Department of Neurology (Acting Head Doc. O. Berg) and from the Department of Otolaryngology (Head Prof. Hj. Koch), University of Lund

Twenty cases of congenital idiopathic nystagmus and twenty one cases of blindness without complicating disabilities were all irrigated with water of 30° and 44°C in the right and the left ear for 40 seconds. The resulting vestibulo ocular and vestibulo spinal reactions were recorded and the experienced vertigo noted.

From earlier examinations it was known that none of these cases of congenital nystagmus had any vestibulo-ocular reactions. Of the blind subjects, 12 cases had no vestibulo ocular reflexes and 9 had weak ones. All cases of congenital nystagmus and blindness had preserved vestibulo-spinal reactions (laterotorsion).

When comparing laterotorsion and vertigo in the two materials with the same qualities in a normal material it was shown that the vestibulo spinal reactions were smaller in cases of blindness with absent vestibulo ocular reactivity than in the other groups and that the vertigo was less in congenital nystagmus than in the other groups.

The similarity of the labyrinthine reactivity pattern in cases of congenital nystagmus and of blindness to that in normals, habituated by repeated calorizations, was pointed out. The possibility that the vestibulo ocular areflexia in congenital nystagmus and blindness might be caused by habituation was discussed.

INTRODUCTION

In a study of congenital idiopathic nystagmus the author (Forssman, 1963b) recently reported that among 88 cases, calorically examined, the vestibulo ocular reflexes were totally abolished in 39 patients and preserved in 40 cases. The reactions were difficult to interpret in the remaining 9 cases. The audiograms were essentially normal in the material and the [illegible] ocular reflexes the author, in collaboration with Henriksson and Dolowitz (Henriksson, Dolowitz & Forssman, 1962), worked out a new method for recording of vestibulo spinal reactions (laterotorsion).

This method was applied to a further study of cases of congenital nystagmus together with a simultaneous recording of the eye movements and also with an

This investigation was supported by the Medical Faculty, University of Lund.

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In langdauernden Fällen ist eine Tracheotomie ratsam, eventuell durch Überdruckventilation ergänzt, manuell oder mittels eines Respirators ausgeführt.

Die Vorzüge und Nachteile der Behandlung werden erwähnt.

Die Überdruckventilation ist als eine „Überlebenstherapie" anzusehen, bei der man die Möglichkeit hat, Zeit zu gewinnen, bis eine Bekämpfung des zugrundeliegenden Leidens mit anderen spezifischen Mitteln möglich wird.

RÉSUMÉ

Rapportant l'observation d'un enfant de deux mois, les auteurs décrivent les moyens dont on dispose pour le traitement des enfants atteints de dépression respiratoire de différentes étiologies.

Si le traitement conservateur: pharmacothérapie, oxygène alvéolaire, hydratation, physiothérapie pulmonaire, ne suffit pas, ils recommendent l'intubation avec aspiration soigneuse des sécrétions et apport éventuel d'air enrichi en oxygène.

Dans les cas où l'affection se prolonge, la trachéotomie est conseillée, complétée au besoin par la ventilation en hyperpression, pratiquée manuellement ou à l'aide d'un respirateur.

Les auteurs rendent compte des avantages et des inconvénients du traitement.

La ventilation en hyperpression est considerée comme une «thérapeutique de survie» permettant de gagner le temps nécessaire pour vaincre, par un traitement spécifique, l'affection causale.

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Copenhagen County Hospital, Gentofte, Denmark

Received June 19, 1963

Alleram & Varga examined 83 blind persons with respect to hearing capacity and to vestibular reactions by cupulometry. As to the rotatory reactions they remarked that only the after sensation could be evaluated because the nystagmus reactions were so weak that they could not be ascertained.

MATERIAL

I Congenital nystagmus

In the recently reported material of congenital nystagmus (Forssman 1963b) 20 of those patients who did not show vestibulo ocular reflexes were examined again with methods to be described below.

Out of the 20 cases 15 were men aged 11–57 years and 5 women aged 27–37 years.

They were all healthy except two who suffered from the following diseases.

Case no 89 ♀ 35 years old. Debility. Since 22 years of age periods of psychic insufficiency and increasing hearing loss probably of hereditary nature.

Case no 91 ♂ 11 years old. Debility. Cerebral atrophy according to pneumoencephalography.

Neurological examinations of all cases were normal except failing muscle stretch reflexes in the legs and weak ones in the arms in case no 89.

All cases were examined by pure tone audiometry, one of them also by speech audiometry. The results were normal with the following exceptions. Two cases showed inner ear hearing loss probably induced by noise. Three cases exhibited conductive hearing loss. One case showed a confusing hearing loss probably of perceptive type.

The eyes of all cases were examined by experts on ophthalmological diseases. The results of these examinations were included in the greater material of congenital nystagmus reported by the author (Forssman 1963b).

II Blindness

In this paper a person is considered blind when his visual acuity is less than 2/60.

Twenty one persons were examined, 15 men aged 27–66 years and 6 women aged 28–61 years.

Only cases with no complicating disabilities were included. In other respects the material was unselected. They were all socially well adapted and active in trade work.

Neurological examination was normal in each case.

All cases except two were examined by tone audiometry, one of them also by speech audiometry. The results were normal except that 6 of them showed inner ear hearing loss probably induced by noise.

All cases had been examined by specialists on ophthalmological diseases. Of the data of these collected examinations sex, age at the author's examination, ophthalmological diagnosis, degree of vision and years of blindness are listed in table I.

estimation of the experienced vertigo. It was hoped that a better understanding of the vestibular reactivity in congenital nystagmus would be made possible by such a procedure.

Some cases of blindness, examined calorically by the author, were tentatively found to lack vestibulo-ocular reactions Because of the striking similarity in this respect to congenital nystagmus, the study was extended to include cases of blindness These were studied by the same methods as those applied to congenital nystagmus for the purpose of studying possible similarities and differences in the pattern of vestibular reactivity in the two materials

For comparison two materials of normals were used. The one was examined in the same way as the cases of congenital nystagmus and blindness, identical with the material described by Henriksson, Forssman & Dolowitz (1962) The other was habituated by repeated calorizations (Forssman, Henriksson & Dolowitz, 1963, Forssman, 1963a), which implied a greater reduction, and even abolishment, of nystagmus and vertigo than of laterotorsion, which could almost always be clearly demonstrated

Aim of the investigation

The aim of the present study was

(1) to establish the pattern of vestibular reactivity in cases of congenital nystagmus and blindness, and

(2) to find out in which respects these patterns differ from or resemble those of normals, habituated resp examined in the same way

HISTORY

A review of the literature on the vestibulo ocular reactions in congenital nystagmus was recently given by the author (Forssman, 1963b) As regards other evoked reactions, Suzuki (1961) reports from a study of pendular nystagmus that dizziness from labyrinthine stimulation did not appear or was minimal in the majority of cases and that vestibulo spinal reactions were present

Vestibular reactivity in cases of blindness has been reported by Igersheimer (1914) and by Alleram & Varga (1957)

Using cold calorization and rotation, Igersheimer examined 10 patients with retinitis pigmentosa The visual acuity was less than 2/60 on the better eye in all cases except two, of which one had 0 25 and the other 0 20 on the better eye The hearing examinations were normal

One case had neither caloric nor rotatory nystagmus reactions, two cases no caloric but normal rotatory responses, one case doubtful caloric and rotatory reactions, five cases weak caloric and normal rotatory responses, and one case normal caloric and rotatory reactions The sensation of dizziness from the vestibular examinations was usually less than normal and totally abolished in some cases

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All cases had been examined by specialists on ophthalmological diseases. Of the data of these collected examinations sex, age at the author's examination, ophthalmological diagnosis, degree of vision and years of blindness are listed in table 1.

TABLE 1 *Sex, age in years at author's examination, ophthalmological diagnosis, degree of vision, and years of blindness of the material*

0 = total amaurosis P = perception of light only L = ability to localize the source of light def = deficiency in this respect H = hand movements F = finger counting N = normal or almost normal vision Index figure denotes the patient's age in years when the assigned degree of vision was established ($0_{<30}$ for example means that amaurosis was established at 30 years of age although is had presumably existed before for an unknown time) In the "Vision" column there are two rows the upper referring to the right and the lower to the left eye The last noted degree of vision was also found at the time of examination In the "Years of blindness" column are listed the minimum number of years during which the visual acuity of both eyes had been less than $^{3}/_{60}$ Heredoretinopathia congenitalis (Alström & Olson 1957) is an atypical pigmentary retinopathy (cf François 1961)

Case no	Sex	Age	Diagnosis	Vision	Years of blindness
1	♂	13	Microphthalmia	$<N_0$ 0.2_{19} $H_{<26}$ $P+$def $L_{<34}$ P_{43} 0_0	1[illegible]
2	♂	30	Heredoretinopathia congen.	$<N_0$ 0 $<N_0$ $0_{<7}$	23
3	♂	38	Glaucoma congen.	$<N_0$ $0.2_{<13}$ $P_{<14}$ 0 [illegible] $<N_0$ $<0.2_{<13}$ $1/60_{<14}$ H [illegible] 0 [illegible]	24
4	♂	[illegible]	Heredoretinopathia congen.	$<N_0$ $0_{<}$ $<N_0$ $0_{<}$	48
5	♀	44	Glaucoma congen.	$<N_0$ $0.1_{<}$ $P+L_{18}$ 0 [illegible] $<N_0$ $0.1_{<}$ $P+L_{18}$ P_{30}	26
6	♂	45	Ablatio retinae + Glaucoma + Retinitis pigmentosa	$<N_7$ $2.5/60_{<10}$ $H_{<1}$ P $_{41}$ 0 $_{45}$ $<N$ $H_{<19}$ P $_{1}$ 0 $_{31}$	25
7	♂	44	Glaucoma congen.	$<N$ $1/60_{18}$ 0_0 $<N$ $1/60_{<18}$ 0_0	48
8		36	*Blenorrhoea neonat.*	$<N_0$ 0_9 N_0 0_9	27
9	♂	40	Heredoretinopathia congen.	P_8 P_0	40
10	♂	56	Heredoretinopathia congen.	N_0 P N_0 P	49
11	♀	51	Heredoretinopathia congen.	$<N_0$ H $_{10}$ P def L P $_{45}$ $<N_0$ H $_{10}$ P def L L $_{45}$	39
12	♂	27	Glaucoma congen.	$<N_{4-10}$ H_9 P L 0 [illegible] N_{4-10} 0_9	18
13	♂	31	Glaucoma congen.	N_0 P_8 0_{18} $<N_0$ 0.8_8 2/60 0_{18}	[illegible]
14	♂	50	Retinitis pigmentosa	$<N_9$ $3/60_{14}$ $L+L_{25}$ $<N_9$ $3/60_{14}$ $P+L_{25}$	
15	♀	2[illegible]	Retinitis pigmentosa	0.2_{19} 0_{29} 0.2_{19} $P+$def L_{21} 0_{29}	[illegible]1
16	♂	53	Iridocyclitis c. cataract. et glaucom. + Retinitis proliferans occ. sin.	P_{20} 0_0 0.1_{20} 2/60 0_{29}	[illegible]1

Table 1 (continued)

Case no	Sex	Age	Diagnosis	Vision	Years of blindness
17	♂	60	Uveitis chron	$\searrow_{39}$ 2 60_{40}, P_{40}, 0_{41}, $\searrow_{39}$, 0 1_{39}, $1/60_{40}$ P_{43}	20
18	♂	42	Vulnus perforans oc sin c ophthalmia sympathica oc dx	$\searrow_{2}$ $<\searrow_{3}$ 0 3_{16} 0 $1/60_{23}$, $P+L_{23}$ P_{40} $\searrow_{2}$ $<\searrow_{3}$ 0 3_{10}, 0 $1/60_{23}$ 0_{23}	20
19	♀	28	Ablatio retinae	$\searrow_{22}$ 0_{22} $\searrow_{22}$ 0_{22}	6
20	♂	41	Uveitis chron	$\searrow_{27}$, $<\searrow_{28}$ 0 3_{30}, 2 60_{35} F_{38} $\searrow_{30}$ 0 7_{30} $0_{<3}$	3
21	♀	61	Retinitis pigmentosa	$<\searrow_{25}$, $H_{<39}$, P_{41} $0_{<51}$ $<\searrow_{25}$, $H_{<39}$ P_{41}, $0_{<51}$	22

METHODS

Methods for vestibular examinations

Every patient was exposed to four caloric irrigations, each during 40 seconds according to the following scheme 30°C right, 30°C left, 44°C right, and 44°C left ear canal The eyes were open The calorizations were performed in darkness unless the patient was suffering from amaurosis of both eyes

The velocity of eye movements was recorded by the derived technique of Henriksson (1955, 1956)

The laterotorsion being an expression of the cristo spinal reflex, was recorded by the method of Henriksson, Dolowitz & Forssman (1962) and expressed in grammes

The vertigo maximum from each calorization was evaluated by the patient and graded according to Ledvall (1961 a) from 0 to 6 (Henriksson, Forssman & Dolowitz, 1962)

Estimation of vestibulo ocular reaction in cases of blindness

All the cases of blindness, except three, showed spontaneous irregular eye-movements De Kleyn (1939, 1949) and Aschan & Bergstedt (1955) have proved that when a non vestibular form of nystagmus (as in blindness) is combined with a vestibular one, it is possible to distinguish the two forms

The vestibulo ocular reactions were evaluated (1) by direct inspection, (2) from the records

(1) In cases of bilateral amaurosis direct inspection with the aid of Frenzel s glasses was performed simultaneously with the registrations, and, in cases of severe amblyopia as a second trial after the recording in complete darkness The repeated irrigations at this second trial imply the possibility

of some degree of response decline from habituation As a rough estimate the reliability seems, however, to be sufficient.

(2) In evaluating the vestibulo-ocular reactions from the records the author was aware of the fact that in eye-diseases such as the present ones the standing corneo retinal potential could in most of the cases be supposed to be subnormal but hardly totally abolished (Heck & Papst, 1956, Arden, Barrada & Kelsey, 1962) There has, however, been no sign of severe reduction of the corneo-retinal potential in any of the records from the blind persons Thus, the blinkings were properly recorded and when a vestibulo-ocular reaction was present on inspection of the eyes, this reaction was also recorded on the paper

For obvious reasons it was not possible to perform tests of eye-velocity The blind persons either showed no caloric reactions at all or weak reactions

Statistical methods (see e g Fisher, 1958)

The F-test has been used for comparisons between two variances according to the formula $F(n_1-1,\ n_2-1)=\frac{S_1^2}{S_2^2}$, where $(n_1-1,\ n_2-1)$ are degrees of freedom

The t-test has been used for comparisons between two means when the variances can be considered equal according to the formula

$$t=\frac{M_1-M_2}{\sqrt{\frac{S_1^2(n_1-1)+S_2^2(n_2-1)}{n_1+n_2-2}}}\sqrt{\frac{n_1\cdot n_2}{n_1+n_2}}$$

The z-test has been used according to the formula

$$z=\frac{M_1-M_2}{\sqrt{\frac{S_1^2}{n_1}+\frac{S_2^2}{n_2}}}$$

for comparison between two means, 1) when the variances cannot be considered equal, and 2) when the single observation does not follow the normal distribution but the mean of more than 30 observations apparently does

The standard deviation within individuals has been denoted S_w and that between individuals S_b The variation coefficients, V, have been correspondingly denoted $V_w=100\ S_w/M$ and $V_b=100\ S_b/M$

Statistical terminology a difference was said to be significant*, significant**, or significant*** when the corresponding P-value was equal to or less than 5, 1, or 0 1 per cent, respectively When P was greater than 5 per cent, the difference was regarded as not significant, denoted ( )

RESULTS

A The experimental data

I Congenital nystagmus

None of the 20 cases had any vestibulo-ocular reflexes according to the selection of the material This areflexia was confirmed in the present study

TABLE 2 *Maximum laterotorsion and maximum vertigo of 20 cases of congenital nystagmus, each irrigated with water of 30°C and 44°C in the right and the left ear*

Calorizations were performed on the left ear only in case no 28 because of an acute otitis of the right ear Case no 89 was examined earlier than the time when estimation of vertigo was introduced. *M* = mean value *S* standard deviation, *n* = number of observations

Case no	Max laterotorsion in grammes				Max vertigo in degrees of vertigo			
	30°C		44°C		30°C		44°C	
	Rt	Lt	Rt	Lt	Rt	Lt	Rt	Lt
6	1276	406	1102	1508	0	0	3	0
7	261	203	348	464	0	0	0	0
8	1740	1044	1102	1566	4	3	3	3
10	348	174	696	406	4	4	3	3
15	464	580	580	638	0	0	0	0
21	406	580	232	232	3	1	3	0
25	638	1160	928	464	1	1	3	3
27	580	232	232	580	0	2	0	1
28		464		696		1		4
29	928	1624	1450	1624	0	0	0	2
31	464	609	1102	464	0	2	2	2
33	406	696	812	696	0	1	2	1
37	1160	696	464	580	0	0	2	2
39	696	696	696	754	0	0	0	0
52	870	232	638	290	5	6	2	3
53	0	812	812	290	0	0	0	0
88	812	232	290	522	0	0	2	1
89	464	580	348	232				
90	1276	1044	1334	1044	3	4	2	3
91	348	754	928	870	0	0	4	6
n	19	20	19	20	18	19	18	19
M	691	641	742	696	1 1	1 3	1 7	1 9
n			78			78		
M			692			1 5		
S			395			1 7		

The spontaneous laterotorsion values were all within the normal range (Henriksson Forssman & Dolowitz 1962) The values for calorically induced laterotorsion and vertigo are given in table 2

As is evident from table 2 all patients showed vestibulo spinal reflexes and these always occurred in the expected direction Fig 1 illustrates a case with no change of the congenital nystagmus but with clear cut laterotorsion on calorization

II Blindness

The material has been divided into two groups according to the absence or presence of vestibulo ocular reflexes

of some degree of response decline from habituation. As a rough estimate the reliability seems, however, to be sufficient

(2) In evaluating the vestibulo-ocular reactions from the records the author was aware of the fact that in eye-diseases such as the present ones the standing corneo-retinal potential could in most of the cases be supposed to be subnormal but hardly totally abolished (Heck & Papst, 1956, Arden, Barrada & Kelsey, 1962) There has, however, been no sign of severe reduction of the corneo-retinal potential in any of the records from the blind persons Thus, the blinkings were properly recorded and when a vestibulo-ocular reaction was present on inspection of the eyes, this reaction was also recorded on the paper

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The z-test has been used according to the formula

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for comparison between two means, 1) when the variances cannot be considered equal, and 2) when the single observation does not follow the normal distribution but the mean of more than 30 observations apparently does

The standard deviation within individuals has been denoted S_w and that between individuals S_b The variation coefficients, V, have been correspondingly denoted $V_w=100\ S_w/M$ and $V_b=100\ S_b/M$

Statistical terminology a difference was said to be significant*, significant**, or significant*** when the corresponding P-value was equal to or less than 5, 1, or 0 1 per cent, respectively When P was greater than 5 per cent, the difference was regarded as not significant, denoted( )

RESULTS

A The experimental data

I Congenital nystagmus

None of the 20 cases had any vestibulo ocular reflexes according to the selection of the material This areflexia was confirmed in the present study

TABLE 3 Maximum laterotorsion and maximum vertigo in 21 cases of blindness each irrigated with water of 30°C and 44°C in the right and the left ear

Group I absent and group II preserved vestibulo ocular reflexes M = mean value S = standard deviation n number of observations

Case no	Max laterotorsion in grammes				Max vertigo in degrees of vertigo			
	30 C		44 C		30 C		44 C	
	Rt	Lt	Rt	Lt	Rt	Lt	Rt	Lt
				GROUP I				
1	307	12	383	5 4	1 0	1 0	1 0	3 0
2	203	522	580	325	3 0	3 0	3 0	3 0
3	534	1	191	30	2 0	2 0	2 0	2 0
4	25	824	02	1038	1 0	1 0	2 0	2 0
5	295	354	4	20	0	0	2 0	2 0
6	148	413	207	1 7	4 0	4 0	2 0	4 0
	944	354	885	08	1 0	1 0	3 0	2 0
8	295	472	413	413	4 0	4 0	3 0	4 0
9	406	522	464	696	3 0	0	3 0	3 0
10	08	826	08	413	2 0	1 0	4 0	1 0
11	54	493	389	447	4 0	3 0	3 0	4 0
12	590	354	354	1 7	3 5	3 5	4 5	4 5
n	12	12	12	12	12	12	12	12
M	475	505	4 9	457	2 4	2 2	2 7	2 9
n			48			48		
M			4 9			2 5		
S			224			1 2		
				GROUP II				
13	1 7	67	95	531	0	2 0	0	1 0
14	1239	531	885	6	0	4 0	3 5	3 5
15	14 5	885	08	413	3 0	3	3 0	4 0
16	1062	1180	1003	08	4 0	4 5	4 5	4 0
1	2262	8 0	1566	1682	3 0	3 0	3 0	5 0
18	1180	6	1121	944	2 0	4 0	3 0	3 0
9	67	236	590	08	4 0	4 0	4 0	4 0
20	531	649	354	118	3 5	4 0	3 5	4 0
2	2191	8 2	52	3248	1 0	1 0	6 0	5 0
n	9	9	9	9	9	9	9	9
M	1243	744	83	1013	2 3	3 3	3 4	3 7
n			36			36		
M			946			3 2		
S			654			1 4		
				GROUP I II				
n			84			84		
M			6 9			2 8		
S			512			1 3		

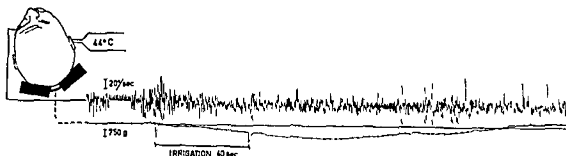


Fig 1 Simultaneous recording of nystagmus and laterotorsion from calorization of a case of congenital nystagmus No change of the congenital nystagmus (upper curve, eye velocity) but a clear cut laterotorsion in the expected direction to the left (deflexion downwards from the base line) (Case no 29)

Group I 12 cases The group comprised those patients who did not show vestibulo-ocular reflexes on calorization None of the first 9 cases exhibited any vestibulo ocular reactions on any of the four calorizations Cases 10, 11, and 12 showed no vestibulo ocular reactions on some of the irrigations and *doubtful ones on the others*

Group II 9 cases, all showing weak vestibulo ocular reactions on all calorizations

The spontaneous laterotorsion values were within the normal range in all cases except no 1, who exhibited spontaneous values to the left of 69 g after one and 156 g after two minutes, thus exceeding the limit for normality with 34 and 56 per cent, respectively

The values for calorically induced laterotorsion and vertigo are given in table 3

All patients showed vestibulo-spinal reflexes and these always occurred in the expected directions Fig 2 illustrates a case with no changes of the spontaneous eye movements but with clear cut laterotorsion on calorization

B Analysis of the experimental data

The figures of the two materials have been compared with those of a normal material of 25 cases, examined in the same way and in the same laboratory (Henriksson, Forssman & Dolowitz, 1962) The blind group I and group II have also been mutually compared Finally a comparison has been made between congenital nystagmus and blinds with absent vestibulo ocular reactions

The reliability of conclusions regarding vertigo is somewhat restricted because of the limited and not equidistant evaluation scale of this quality (Lidvall, 1961 b)

The conclusions below refer to the present materials only

I Congenital nystagmus

a) *Laterotorsion* There is no significant difference in the mean values between normals and cases of congenital nystagmus, according to the z test $z = 1.63^{(-)}$

Conclusion There is a suggestion that cases of blindness with non existent vestibulo ocular reflexes become less dizzy from vestibular stimulation than those with preserved vestibulo ocular reflexes

2) *Comparison with the normal material*

a) *Laterotorsion* There is no significant difference between the total mean value of the blind (group I + group II) and the mean value of normals = 1 66)

The mean value of blind group I is, however, significantly*** smaller than that of the normals z = −4 52***

The standard deviation of all the blind (group I + group II) is significantly** smaller than that of normals *F* (99, 83) = 1 88** The standard deviation of blind group I is significantly*** smaller than that of normals *F* (99, 47) = 9 82***

By comparing the variations within and between the individuals by means of the variation coefficients

	Normals	Blinds		
		Group I + II	Group I	Group II
V_w (per cent)	53	55	41	57
V_b (per cent)	144	119	72	100

it is seen that in all materials the variations are less pronounced within the individuals than between them

The variation within individuals is essentially equal in all the materials, blind group I however, showing a somewhat smaller value

The variations between the individuals is smaller in both group I and group II than in all the blind cases which in turn are smaller than those in normals This implies that group I and group II are more homogeneous than group I + group II which is again more homogeneous than the normals

Conclusions In blindness with preserved vestibulo ocular reflexes the vestibulo spinal reactions are normal

In blindness with absent vestibulo ocular reactions the vestibulo spinal reactions are smaller than normal

The variations in the vestibulo spinal reactions in blind subjects are about normal in all cases The variations of the vestibulo spinal reactions between the blind are somewhat smaller than normal especially when considering the cases with absent and the cases with preserved vestibulo ocular reactivity separately

b) *Vertigo* The values for vertigo only of group I are significantly** lower than in the normal material *t* being −2 97**

Conclusion Cases of blindness with absent vestibulo ocular reflexes become less dizzy from vestibular stimulation than normals

III Comparison between congenital nystagmus and blind group I

Both of these materials lack vestibulo ocular reactions

a) *Laterotorsion* The mean values as well as the standard deviations are



FIG 2 Simultaneous recording of nystagmus and laterotorsion from calorization of a case of blindness No changes of the spontaneous eye movements (upper curve, eye velocity) but a clear cut laterotorsion in the expected direction to the left (deflexion downwards from the base line) (Case no 1)

The standard deviation is significantly* lower in cases of congenital nystagmus than in normals, F (99, 77) being 3 15***

By comparing the variations within and between the individuals by means of the variation coefficients

	Normals	Congenital nystagmus
V_w (per cent)	53	38
V_b (per cent)	144	96

it is seen that in both materials the variations are less pronounced within than between the individuals Both these kinds of variation are, however, smaller in the group with congenital nystagmus than in the normal material

Conclusion In congenital nystagmus with absent vestibulo ocular reactions, the vestibulo spinal reactions are of normal magnitude and show smaller variations than normal

b) *Vertigo* The values for vertigo are significantly*** lower in congenital nystagmus than in the normal material according to the z-test, z being 7 24***

Conclusion Cases of congenital nystagmus with no vestibulo ocular reactivity become less dizzy from vestibular stimulation than normals

II Blindness

1) Comparisons between group I and group II (absent and preserved vestibulo-ocular reflexes)

a) *Laterotorsion* The mean values as well as the standard deviations are significantly*** lower in group I than in group II z for the mean values =4 11*** F (35, 47) for the standard deviations = 8 53***

Conclusion In blind subjects the vestibulo spinal reflexes are weaker when the vestibulo ocular reflexes are also weaker

b) *Vertigo* The values for vertigo of blind group I are significantly* lower than those of group II, *t* being 2 41* Because of the limited reliability of this quality, it may be said that there is only a suggestion of vertigo being less pronounced in blind group I than in blind group II

Conclusion There is a suggestion that cases of blindness with non existent vestibulo ocular reflexes become less dizzy from vestibular stimulation than those with preserved vestibulo ocular reflexes

2) *Comparison with the normal material*

a) *Laterotorsion* There is no significant difference between the total mean value of the blind (group I + group II) and the mean value of normals $t = 1\ 66$

The mean value of blind group I is however, significantly*** smaller than that of the normals $t = 4\ 52$***

The standard deviation of all the blind (group I + group II) is significantly** smaller than that of normals $F\ (99\ 83) = 1\ 88$** The standard deviation of blind group I is significantly*** smaller than that of normals $F\ (99\ 47) = 9\ 82$***

By comparing the variations within and between the individuals by means of the variation coefficients

	Normals	Blinds		
		Group I + II	Group I	Group II
V_w (per cent)	53	55	41	57
V_b (per cent)	144	119	72	100

it is seen that in all materials the variations are less pronounced within the individuals than between them

The variation within individuals is essentially equal in all the materials blind group I however showing a somewhat smaller value

The variations between the individuals is smaller in both group I and group II than in all the blind cases which in turn are smaller than those in normals This implies that group I and group II are more homogeneous than group I + group II which is again more homogeneous than the normals

Conclusions In blindness with preserved vestibulo ocular reflexes the vestibulo spinal reactions are normal

In blindness with absent vestibulo ocular reactions the vestibulo spinal reactions are smaller than normal

The variations in the vestibulo spinal reactions in blind subjects are about normal in all cases The variations of the vestibulo spinal reactions between the blind are somewhat smaller than normal especially when considering the cases with absent and the cases with preserved vestibulo ocular reactivity separately

b) *Vertigo* The values for vertigo only of group I are significantly** lower than in the normal material t being $= 2\ 97$**

Conclusion Cases of blindness with absent vestibulo ocular reflexes become less dizzy from vestibular stimulation than normals

III Comparison between congenital nystagmus and blind group I

Both of these materials lack vestibulo ocular reactions

a) *Laterotorsion* The mean values as well as the standard deviations are



Fig. 2. Simultaneous recording of nystagmus and laterotorsion from calorization of a case of blindness. No changes of the spontaneous eye movements (upper curve: eye velocity) but a clear cut laterotorsion in the expected direction to the left (deflexion downwards from the base line). (Case no. 1.)

The standard deviation is significantly*** lower in cases of congenital nystagmus than in normals, $F_{(99, 77)}$ being 3.15***.

By comparing the variations within and between the individuals by means of the variation coefficients

	Normals	Congenital nystagmus
V_w (per cent)	53	38
V_b (per cent)	144	96

it is seen that in both materials the variations are less pronounced within than between the individuals. Both these kinds of variation are, however, smaller in the group with congenital nystagmus than in the normal material.

Conclusion. In congenital nystagmus with absent vestibulo ocular reactions the vestibulo spinal reactions are of normal magnitude and show smaller variations than normal.

b) *Vertigo.* The values for vertigo are significantly*** lower in congenital nystagmus than in the normal material according to the z test, z being 7.24***.

Conclusion. Cases of congenital nystagmus with no vestibulo ocular reactivity become less dizzy from vestibular stimulation than normals.

II. Blindness

1) Comparisons between group I and group II (absent and preserved vestibulo ocular reflexes).

a) *Laterotorsion.* The mean values as well as the standard deviations are significantly*** lower in group I than in group II, t for the mean values = 4.11***, $F_{(31, 17)}$ for the standard deviations 8.63.

Conclusion. In blind subjects the vestibulo spinal reflexes are weaker when the vestibulo ocular reflexes are also weaker.

b) *Vertigo.* The values for vertigo of blind group I are significantly* lower than those of group II, t being 2.41*. Because of the limited reliability of this quality, it may be said that there is only a suggestion of vertigo being less pronounced in blind group I than in blind group II.

(a) If a basic anatomical change was located in the labyrinth the only possible site would be hypothetical special receptors on the crista specially concerned with cristo ocular reflexes or the first vestibular neurone connected to these receptors (cf Dolowitz Forssman & Henriksson 1962) This is concluded because the results of the hearing acuity examinations are essentially normal and because the cristo spinal reflexes and the sensation of dizziness from vestibular stimulations are preserved

(b) The pathological process might involve the central vestibulo ocular connections With few insignificant exceptions however there are no anamnestic symptoms or clinical neurological signs of central nervous disturbances except vestibulo ocular areflexia

Alternatives (a) and (b) are undoubtedly improbable because they would entail the assumption that the causes which are numerous at least as far as the eye affections are concerned would give rise to a highly selective damage to the hypothetical labyrinthine receptors or their first vestibular neurone and or a circumscribed area of the central nervous system

II Functional disturbance

The results might be explained on a functional basis as habituation phenomena This implies a decline of a response to the monotonous repetition of an indifferent useless or inadequate stimulus Thorpe who regarded habituation as the most simple type of learning defined it (1956) as a simple learning not to respond to stimuli which tend to be without significance in the life of the organism a tendency merely to drop out responses

After (a) a schematic presentation of the purpose of the different sources of and the influences on eye movements the possibility of a habituating mechanism as the cause of some symptoms in (b) congenital nystagmus and (c) blindness will be discussed Finally (d) a comparison will be made with an earlier study of habituated normals

(a) The purpose of the sources of and the influences on eye movements The purpose of the optically voluntarily and vestibularly elicited impulses to the eye muscles is primarily to produce the visual fixation and secondarily also to facilitate the orientation of the subject in space

By way of reflexes passing the occipital area the optically elicited impulses give rise to follow movements The voluntary eye movements also implying movements on command pass from the second frontal convolution to the eye muscles Finally the vestibular eye movements arise from labyrinthine impulses

The impulses to the eye muscles from all these sources are subject to modifying influences comprising both excitatory and inhibitory components mediated by a certain brain stem area (cf Szentagothai & Schab 1956 Lachmann Bergmann & Monnier 1958 Bergmann Lachmann Monnier & Krupp 1959 Bergmann Lachmann Chaimovitz & Gutman 1961) Of special interest are the findings of Szentagothai & Schab namely that

significantly * lower in the blind group I than in congenital nystagmus – for the mean values −3.86 *, F (77.47) for the standard deviations −3.12***.

Conclusions. In blind subjects with absent vestibulo ocular reflexes the vestibulo spinal reflexes are weaker and show smaller variations than these in congenital nystagmus.

b) *Vertigo.* The values of vertigo are significantly** higher for blind group I than for congenital nystagmus −3.91**.

Conclusion. Blind subjects with absent vestibulo ocular reflexes become more dizzy from vestibular stimulation than cases of congenital nystagmus.

Summary of the conclusions

Laterotorsion. Blind group I (absent vestibulo ocular reactions) have smaller laterotorsion values than blind group II (preserved vestibulo ocular reactions), cases of congenital nystagmus and normals, and these three last mentioned groups have about equal laterotorsion values.

The variability of the laterotorsion values within individuals is less pronounced in congenital nystagmus than in blind cases and normals.

The variability of the laterotorsion values between individuals is generally greater in normals than in cases of congenital nystagmus and blindness.

Vertigo. The order of experienced vertigo from vestibular stimulation from greatest to slightest dizziness is

1) Normals equal to blind group II (preserved vestibulo ocular reactions)
2) Blind group I (absent vestibulo ocular reactions)
3) Cases of congenital nystagmus

DISCUSSION

The most remarkable result of a study of congenital nystagmus (Forssman 1963b) was that 39 out of 88 cases showed a vestibulo ocular areflexia.

In the study of the cases of blindness reported in this paper the most remarkable result is no doubt the same, viz. the frequent finding of a vestibulo ocular areflexia.

The question naturally arises if there is a common cause of such areflexia in materials of so different kinds as congenital nystagmus and blindness. From the results of the author's previous and present studies in the field of vestibular reactivity this question will be discussed below from a hypothetical standpoint.

The phenomenon of vestibulo ocular areflexia may have a pathological anatomical basis or be due to functional disturbance.

I. Pathological anatomical considerations

The pathogenetic disturbances which are the causes of congenital nystagmus and blindness might conceivably also give rise to anatomical changes in (a) the labyrinth and/or in (b) the central nervous system.

disappeared but not nystagmus, unless the calorizations were performed in light with laterotorsion almost always present

When the three materials (habituated normals, cases of congenital nystagmus and of blindness) are compared, they have in common the following symptoms weak resp abolished vestibulo ocular reflexes and preserved vestibulo spinal reflexes The picture of vertigo, however, varies

As to the different degrees of depression of the three qualities in the three materials the following facts must be taken into consideration

The source of habituation is different In congenital nystagmus it is the inadequate motion of pictures on the retina which causes a specific habituation —In cases of blindness the habituation has a threefold origin because optically voluntarily and vestibularly induced eye movements are all useless —In repeatedly calorized normals the habituating impulses originate from the labyrinth only

The habituating impulses in cases of congenital nystagmus and blindness are repeated daily over years those of habituated normals only about one hour

These differences in source and duration of the habituating impulses between the three groups may explain the varying degrees of depression of the three qualities

ZUSAMMENFASSUNG

Bei 20 Fallen mit kongenitalem idiopathischen Nystagmus und 21 Blinden ohne weiteren Ausfallserscheinungen wurden Vestibularisuntersuchungen durchgeführt mit Spulung beider Ohren mit 30° und 44°C warmen Wasser in einer Dauer von 40 Sekunden Die vestibulo okularen und vestibulo spinalen Reaktionen wurden registriert und der hervorgerufene Schwindel festgestellt

Von vorhergehenden Untersuchungen war bekannt, dass die 20 Falle mit kongenitalem Nystagmus keine vestibulo okularen Reaktionen aufweisen Unter den Blinden hatten 12 keine und die übrigen 9 schwache vestibulo okulare Reflexe Alle Falle mit kongenitalem Nystagmus und Blindheit hatten dagegen vestibulo spinale Reaktionen (Laterotorsion)

Bei einem Vergleich der Laterotorsion und des Schwindels bei den beiden Gruppen mit den Erscheinungen bei normalen Versuchspersonen konnte gezeigt werden, dass die vestibulo spinalen Reaktionen bei Blinden ohne vestibulo-okularen Reaktionen vermögen geringer sind als bei den anderen Gruppen Es konnte ausserdem festgestellt werden, dass Schwindel bei Fallen mit kongenitalem Nystagmus in geringerem Masse auftritt als bei den Vergleichsgruppen

Es wird die Ähnlichkeit der vestibularen Reaktionsart hervorgehoben zwischen den Fallen mit kongenitalem Nystagmus und Blindheit und normalen Versuchspersonen wenn sich diese an wiederholte kalorische Prüfungen gewohnt haben Es wird weiterhin die Möglichkeit diskutiert, ob die vestibulo okulare Areflexie bei kongenitalem Nystagmus und Blindheit durch Gewohnung zustande kommen kann

vestibulo ocular reflexes can be abolished by stimulation of a midbrain area corresponding to the nucleus of Darkschewitsch

(b) Congenital nystagmus The perpetual eye movements of congenital nystagmus impair the visual fixation and the orientation of the subject in space The objects in the field of vision continuously move on the retina Such a state is apt to give the patient an impression of motion in relation to the surroundings and thereby to produce dizziness The spontaneous eye movements thus being inadequate to the real situation and repeated there are pre requisites for habituation of them and of the consequent vertigo The habituation however is not sufficient to inhibit the spontaneous nystagmus totally but sufficient to depress the subsequent symptoms of these inadequate eye movements oscillopsia and vertigo

The habituation is highly specific (cf Sharpless & Jasper 1956 Groen 1957 Hernandez Peon Jouvet & Scherrer 1957 Hagbarth & Kugelberg 1958) In congenital nystagmus it may be assumed that the habituation is directed to a suppression of only such impulses as give rise to the same effect as the disease viz those which tend to impair the visual fixation and the orientation of the subject in space

Such a specificity of the habituating process might explain why the voluntary and follow movements of the eyes are preserved but the nystagmus from vestibular stimulation abolished

The fact that the vestibulo spinal reflexes are normal on vestibular stimulation in congenital nystagmus is in accordance with the explanation given of the specificity of the habituation

(c) Blindness The purpose of the optically voluntarily and vestibularly elicited impulses to the eye muscles is to effect the visual fixation When blindness ensues the optically elicited impulses are lost and the others become useless There are thus conditions for the habituation of vestibularly and voluntarily induced eye movements There is however no mechanism giving the impression of bodily motion as in congenital nystagmus and therefore there is no habituation of vertigo

In accordance with such a theory the vestibulo ocular areflexia can be explained as can also the frequently found difficulty of performing eye movements on command (not systematically investigated)

It is difficult to explain that laterotorsion of the blind subjects with absent vestibulo ocular reflexes is depressed but not that of those with these reflexes preserved It may be that a more pronounced habituation as expressed by a greater depression of eye movements is also extended to the vestibulo spinal reflexes

(d) The experimental studies of habituation which will be used for a comparison with the results of this paper have recently been reported by Forssman Henriksson & Dolowitz (1963) and by Forssman (1963a) The repeated monoaural isotermal calorizations entailed a habituation of vertigo nystagmus and laterotorsion in that order from the greatest to the slightest response decline At the end of the irrigations vertigo had usually

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The method has been of special value in cases of tumours, especially glomus tumours, involving the superior bulb and the upper cervical part of the vein (Gejrot & Lauren, 1964)

As the examination is relatively easy to perform and causes only moderate discomfort, the indications can be wide, 80 such examinations have been made to date

The increased usefulness of the method gives reasons for a more detailed description of the technique and normal findings than was possible in the preliminary report by Gejrot and Lindbom This is the purpose of the paper

Anatomy

The main venous return from the brain is via the internal jugular veins (Fig 1) These begin as direct continuations of the sigmoid sinuses, with a more or less dome shaped widening the superior bulb The dome is usually separated from middle ear by a bony wall The average width of the jugular vein and the transverse sigmoid sinus is greater on the right side The transverse sinuses join in the midline of the occipital bone, forming the torcular Herophili, which receives blood from the superior sagittal sinus and the rectal sinus The anatomic variations of the torcular have been classified by Woodhall into four types, namely plexiform, common pool, ipsilateral and unilateral In the ipsilateral type the superior sagittal sinus empties into one transverse sinus, usually the right, and the rectal sinus into the other In these cases the right and left transverse sinuses may be connected only by a canal of varying width In the unilateral type the superior sagittal and rectal sinus empty into one transverse sinus

Aplasia of one transverse sinus and jugular vein has been reported by many authors

The fact that the cranial sinuses and the upper part of the jugular veins contain *no valves* facilitates the retrograde injection of contrast medium

Besides the jugular veins the following auxiliary venous channels contribute to the drainage and may be of vital importance if the flow in the jugular veins is suddenly impaired the pharyngeal and pterygoid plexus the vertebral and occipital plexus the ophthalmic veins, extracranial connections via the diploic system and the emissary veins (Fig 1) The most important emissary veins are the parietal, occipital and mastoid, the veins of the posterior and anterior condylar canals and the venous plexus surrounding the third trigeminal branch through the foramen ovale and the plexus in the carotid canal The width of these venous channels [illegible] greatly

The [illegible]

bones [illegible] by the intrajugular process of the occipital bone into a postero lateral portion through which passes the internal jugular vein, and an anterior portion giving passage to the IX, X and XI cranial nerves and the inferior petrosal sinus The venous portion has the form of a short, curved canal having a distal and forward direction the opening is oval in shape

The upper part of the jugular vein s cervical portion has the following anatomical relations Posteriorly are the transverse process of atlas and the ventral and lateral rectus capitis muscles Ventro medially the vein is related to the internal carotid artery Laterally are the styloid process, stylohyoid muscle and posterior portion of

RETROGRADE VENOGRAPHY OF THE INTERNAL JUGULAR VEINS AND TRANSVERSE SINUSES

Technique and roentgen anatomy

TOMAS GEJROT and TORE LAURÉN
Stockholm, Sweden

From the Department of Oto rhino laryngology (Head C-A Hamberger) and the Central Department of Diagnostic Radiology (Head K Lindblom), Karolinska Sjukhuset, Stockholm 60

A detailed description of the technique of retrograde jugularography and of the normal variations of the transverse sinus and internal jugular vein is given The value of the method for preoperative examination of the venous drainage from the brain is discussed The variations of the contours of the upper part of the internal jugular vein are described and the usefulness of retrograde jugularography in diagnosing tumours in or around the jugular foramen is emphasized

The venous return from the brain was earlier studied by means of carotid angiography or venography in the direction of the blood stream, or simply by measuring the transverse and sigmoid grooves and the jugular foramina By carotid angiography it is possible to visualize the veins and dural sinuses, but the maximum dose of contrast medium is too small for distinct opacification of the jugular veins especially their upper part which is covered by the temporal bone In venography a much higher dose can be given without risk of impairing the cerebral circulation Sinography after trephination of the sagittal sinus was introduced by Frenckner in 1934, who found it valuable for demonstrating sinus thrombosis Romieu *et al* (1959) and Bienas (1962) examined the jugular veins by means of percutaneous puncture and injection of contrast medium into the upper bulb Attempts have also been made to study the jugular veins by injecting medium into the ophthalmic facial and temporal veins (Romieu *et al*) With Frenckner s method the sinuses and the jugular veins are clearly visualized, but the trephination complicates the examination It is, however, still the best with regard to the confluens and posterior part of the superior sagittal series

The jugular venography by retrograde catheterization was introduced by Gejrot and Lindbom in 1959, and 20 cases in which it was used were reported in 1960 The primary aim was to study the venous drainage from the skull before neck dissection and to visualize impressions in the veins caused by tumours and metastases Cases of anomalous superior bulbs have also been reported (Gejrot, 1964)

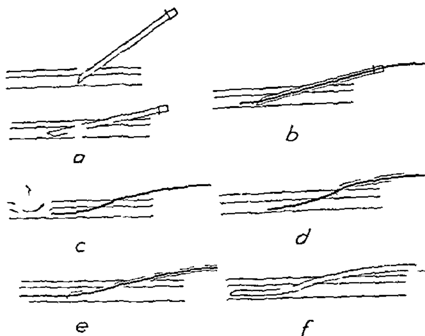


Fig 3 Diagram of the Seldinger technique (a) The vessel punctured (b) the leader inserted (c) the needle withdrawn and the vessel compressed (d) the catheter threaded on to the leader (e) the catheter inserted into the vein (f) the leader withdrawn (After Seldinger S I 1953 Catheter replacement of the needle in percutaneous arteriography *Acta Rad ol 39 368*)

about 3 seconds) The compression can be obtained either manually (lead rubber gloves!) or by means of a rubber sling from the opposite axilla Three or four films are exposed in rapid succession the first exposure being made just before the end of injection Either a simple manual cassette changer or an Elema Schonander serial apparatus was used

Two routine projections were used the antero posterior view with the tube 35° towards the feet and the lateral view with the head slightly rotated in order to avoid overprojection from the contralateral side In some cases additional films were taken in axial or Stenver s projections The soft catheter enables the head to be moved freely and many projections to be used Four or five injections can be made without exceeding the maximum dose

After the examination the patient is raised to the half sitting position the catheter is withdrawn and moderate compression applied for some minutes

In general the examination was well tolerated by the patients The discomfort of the injection was mild and of short duration except in two cases of the whole series when the injection caused severe half sided headache which lasted for about one minute In both these cases the venous drainage was greatly obstructed on the other side and the pain was probably caused by a sudden raise in intracranial pressure In one case there was a brief

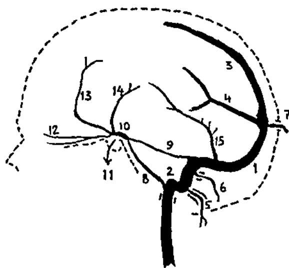


Fig. 1



Fig. 2

Fig. 1. *1* Transverse sinus, *2* Superior bulbus, *3* Superior sagittal sinus, *4* Rectal sinus, *5* Emissary vein through posterior condylar canal, *6* Mastoid emissary vein, *7* Occipital emissary vein, *8* Inferior petrosal sinus, *9* Superior petrosal sinus, *10* Cavernous sinus, *11* Connections between cavernous sinus and pterygoid and pharyngeal plexus, *12* Ophthalmic vein, *13* Sphenoparietal sinus, *14* Middle cerebral vein, *15* Inferior anastomosing vein (Labbé) connecting middle cerebral vein with transverse sinus.

Fig. 2. *1* Nervous, and *2* Venous part of the jugular foramen, *3* Intrajugular process, *4* Clivus, *5* Occipital foramen.

the digastric muscle. In its lower course the vein is covered laterally for its whole length by the sternocleidomastoid muscle.

Technique

The patient lies in the supine position with the head bent slightly backwards. The common carotid artery and the anterior margin of the sternocleidomastoid muscle are located and their point of intersection marked on the skin. After inducing local anesthesia without vasopressor drug the skin is punctured at this point with a no. 205 Seldinger needle. The vein is usually found without difficulty one centimetre lateral to the artery. It is important to instruct the patient to perform the Valsalva manœuvre so as to distend the vein during puncture, moreover, the needle should be placed accurately in the axial direction of the vessel. A pillow under the patient's shoulders facilitates the puncture. The needle is then replaced by a no. 205 polythene catheter using Seldinger's method (see Fig. 3). The tip of the catheter is placed in or just below the bulb. Before attaching the catheter to the skin, physiologic saline is injected: this usually causes a sensation of cold and tension in the ear. Injection and aspiration should be encountered without resistance.

While applying pressure to the vein distal to the site of injection 25–30 ml of 45 % Urografin is injected with the maximum manual pressure (taking



Fig 5 A



Fig 5 *B*

Fig. 5. Injection from the right side. Right and left jugular veins approximately equal. Note the irregularity of the right transverse sinus. Ordinary filling of vertebral and occipital plexuses. Small amount of contrast medium in cavernous sinus (↓) via inferior petrosal sinuses (↕). A Antero posterior view. *B* lateral view.



Fig. 1. Retrograde jugularography from the right side with good filling of the left side via the torcular Herophili. Antero-posterior view. Right jugular vein and transverse sinus wider than left.

allergic reaction to the contrast medium. In one case the common carotid artery was punctured by mistake, and a haematoma resulted.

When the catheter is pushed upwards it is usually arrested by the dome of the bulb. In two cases, however, it passed unresisted into the sigmoid sinus, and in another two cases into unusually wide inferior petrosal sinuses. This did not cause any extraordinary sensations.

The examination is seldom difficult to perform. Difficulty in finding the vein is, in our experience, due mostly to an inadequate Valsalva manoeuvre. The effect can be intensified by tilting the table. If the puncture still does not succeed, the vein is probably narrow and the other side should be tried. In all we failed to puncture the vein in three cases.

Material

Thirty-eight of the 80 cases could be regarded as normal so far as the venous pathways from the skull were concerned. In one case the examination was unsuccessful because the vein could not be found, and as there was no urgent need for the examination we did not try on the other side. In



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Fig 5 *B*

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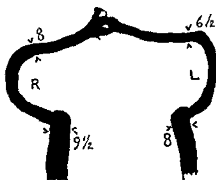


FIG 7 Mean values of transverse sinus and jugular veins

some cases the injection had to be repeated after adjusting the position of the catheter The passage was difficult if not impossible to obtain when the vein was unusually wide or when the collaterals to the vertebral and sub occipital plexuses were extraordinary well developed

I NORMAL FINDINGS AND VARIATIONS OF THE INTERNAL JUGULAR VEINS AND THE TRANSVERSE SINUSES

In our series we found the following relations between the transverse sinuses and the jugular veins

	No of cases
Right jugular vein wider than the left	13
Left jugular vein wider than the right	6
Right and left jugular veins approximately equal	9
(Doubtful because of poor filling	8)
Right transverse sinus wider than the left	10
Left transverse sinus wider than the right	4
Right and left transverse sinuses approximately equal	9
(Doubtful because of poor filling or irregular contour	13)

It was possible to measure the size in most cases at least in the antero posterior projections The transverse sinuses were mostly measured sym metrically in the lateral part If the sinuses were irregular the average of three symmetrical points were taken (If very irregular no measurements were made)

The jugular veins were measured in or immediately below the foramen (Fig 7) The following values were found

	Average mm	Range	Values
Right jugular vein	9 5	6 16	(33)
Left jugular vein	8	5 13	(31)
Right transverse sinus	8	5 12	(31)
Left transverse sinus	6 5	3 12	(25)



Fig. 6. Injection from the left side. Left jugular vein wider than right. A vein empties into the left transverse sinus (↓).

another case the examination was discontinued because of an allergic reaction to the contrast medium.

The remaining 36 cases provided the following clinical findings:

Carcinoma of the external ear, oral or nasal cavity, nasopharynx or larynx with no signs of metastases or suspected palpatory findings that could not be verified at the subsequent neck dissection: 13 cases.

Tumours of the salivary glands without metastases or with small metastases, that were found at operation not to be related to the vein: three cases.

Malignant melanoma, with no metastases near the jugular vein at operation: two cases.

Menière's disease: four cases.

Uncomplicated chronic otitis: four cases.

Single cases of zygomatic fracture, acoustic neurinoma, osteitis of the mandibular joint, otosclerosis, chronic laryngitis, tinnitus, small haemangioma in the forehead, haematotympanum (no visible fracture, negative exploration of the tympanic cavity), acromegaly (without bone destruction in the sella), and chronic, nonspecific lymphadenitis.

Results

Passage of contrast medium via the torcular Herophili to the other side was obtained in 28 cases, sometimes only a small amount (Figs. 4–6). In

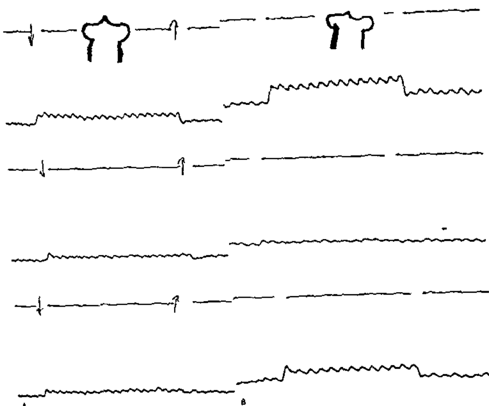


Fig. 9. Records of lumbar pressure on compressing (↓) both internal jugular veins (top) and left and right vein (adjacent). A. Equally large veins. *B.* Insufficiency of left internal jugular vein.

The interest in this field has been stimulated by the circulatory problems in sinus thrombosis and (subsequent) radical neck dissection. In cases of anomalous drainage several severe complications, even death, have been reported sequelae of excision of the internal jugular vein (Ersner & Myers, 1933. Mayfield 1941. Diamant & Forsberg 1957. Morfit, 1957).

The dominance of the right side was recognized by Hunauld (1730) and Morgagni (1741). In comparative anatomical studies on cadavers Rudinger (1875) and Koerner (1886) found that the groove of the right transverse sinus was generally deeper than that of the left—in 75 per cent of Koerner's cases. This was ascribed to the fact that the major part of the venous blood from the superior sagittal sinus is drained through the right transverse sinus. Ulrich (1900) also found that the right transverse sinus was more strongly developed than the left in 65 per cent of cases. X-ray examination of the transverse sulcus was introduced by Ersner & Myers (1933). In measurements of the width in a large number of normal subjects, they found no uniformity. Thus the right sulcus was wider than the left in 89 per cent of the cases. Similar results were obtained by Berg & Constans (1933).

The same applies to the jugular foramen which as a rule is larger on the



Fig 8 A



Fig 8 B

Fig 8 Injections from the right side The transverse sinus is wider than the jugular vein Wide posterior condylar emissary vein (↓) vertebral plexus (↕) and deep dorsal vein (⚲) *A* Lateral view *B* antero posterior view

As the postero lateral part of the jugular foramen contains nothing but the vein a close correspondence would be expected between the upper part of the vein and the foramen The difference between the width of the foramen according to Lindblom (1936) and the width of the vein in our series was about 3 5 mm (right 3 4 and left 3 6 mm), a value that seems to correspond to the thickness of the wall

The transverse sinus was usually a little narrower than the jugular vein on the same side, except in one case, where the relationship was reversed This seemed to be compensated for by an unusually wide posterior condylar emissary vein and a plexus of veins in the vertebral and suboccipital region (Fig 8)

Discussion

Many investigations have been performed to demonstrate the anatomic variations of the venous pathways and the part they play in the drainage

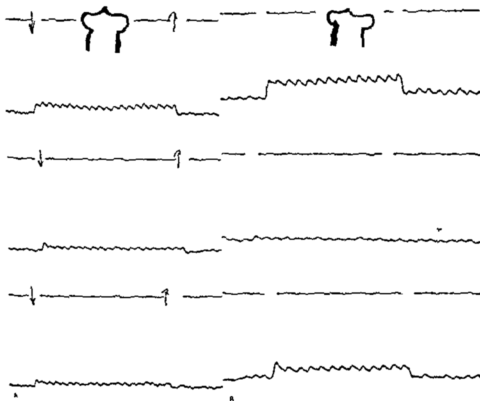


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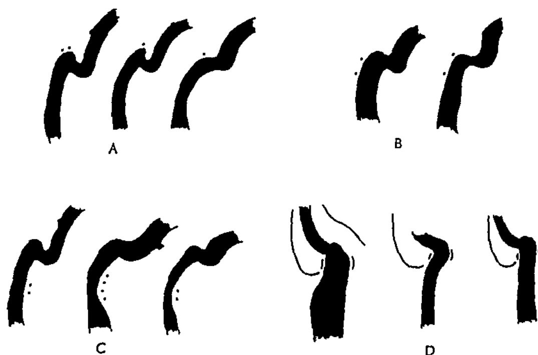


Fig. 10. Normal variations in contour of upper part of jugular vein. *A.* Superior bulbus, *B.* Anterior, and *C.* Posterior contours, *D.* Lateral and medial contours.

right side. Thus, in the 449 skulls studied by Koerner, the right jugular foramen was larger in 58.8 per cent and the left in 24.3 per cent, only 76 skulls (16.9 per cent) having a jugular foramen of the same size on both sides. In 1052 skulls measured by Linser (1900), the corresponding incidence was 62.9, 23.4 and 13.7 per cent, respectively. In 3 per cent of Ersner & Myers' series, an extremely small jugular foramen was present on one side. In one case they found the right jugular foramen to be almost eight times wider then the left. Lindblom (1936) found on rœntgenograms the average of the right jugular foramen to be 12.9 by 8.6 mm and of the left 11.6 by 7.6 mm. Frenckner (1940, 1958) observed a relation between the size of the transverse sinus groove and jugular foramen on the same side. In connection with neck dissection Frenckner (1958) applied sinography in a study of the venous outflow. He found aplasia or hypoplasia of one transverse sinus in 15 out of 30 cases, a difference in size in four cases and the same size bilaterally in 11 cases; he regarded these figures consistent with his earlier findings (1940).

To ascertain the significance of variations in the vein in Queckenstedt's test Minnegerode (1961) compared the increase in lumbar pressure of 186 normal subjects on compressing the right and left internal jugular veins. In only 13.1 per cent of the series was the rise in pressure the same for both veins; in 60.3 per cent the rise was greater for the right vein.

In addition to the rough check of the jugularography findings performed at the subsequent neck dissection, a few comparisons were made of the size of the veins on the radiographs and the increase in pressure on compressing the respective veins. The findings for two typical cases are shown in Fig. 9. The



Fig. 11. Emptying sequence. Viewed along the vein in the middle film seems to be occluded by a tumour (←).

sure is in close agreement with the radiologic findings both in the case of equally large internal jugular veins and in the case of marked assymmetry.

The area of the cross section would of course give a more accurate picture of the venous capacity than one diameter. This is particularly true of the transverse sinuses which are rather irregular in shape. However, approximate measurements seemed to confirm Frenckner's conclusion that before radical neck dissection sufficient information on the venous drainage can usually be gained from plain radiographs of the transverse sulci and/or the jugular foramina. If there is reason to suspect earlier sinus thrombosis or severe impairment of the venous drainage by tumour impression, retrograde jugularography is recommended.

II. Normal Variations in the Contour of the Upper Part of the Internal Jugular Vein

The increase in the number of cases of tumours affecting the temporal bone and the upper part of the internal jugular vein admitted for examination has focused our interest on this region and the normal variations found will therefore be briefly described.

The superior bulb is best seen in lateral view. Three cases of phlebographically verified anomalies have recently been published by Gejrot (1964) and are not included in the normal material. The extreme variations of the shape of the bulb in the present material is demonstrated in the sketches in Fig. 10, which have been traced from the films.

The anterior contour of the vein's cranial part was always found to be uniformly convex within the variations shown in (*B*). The posterior contour (*C*) was in some cases strongly concave. Variations in the shape of the transverse process of atlas and epistropheus may explain these sometimes striking variations. In the antero-posterior view the jugular veins may con-



FIG 12 Filling defect in the anterior wall, probably an artefact caused by the inflow from the common facial vein

verge slightly upwards or run parallel The medial contour is usually smooth, the lateral more irregular and sometimes S shaped (*D*) No attempt was made to study the anatomy in detail and the variations that may be due to changes in head posture

Comments

All phlebograms present dangers of misinterpretation due to incomplete mixing of the blood and contrast medium, which has a tendency to sediment along the lower wall of the vessel In the supine position great care must therefore be taken not to misinterpret irregularities in the anterior wall In addition there are often false filling defects caused by blood entering from branches The sedimentation effect increases with the distance from the site of injection Rapid injection of large volumes of contrast medium and serial exposures lessen the risk of such misinterpretations

The value of serial exposures is illustrated in Fig 11, which shows an atypical sequence of emptying films, taken at intervals of about one second The middle film is suggestive of a blocking tumour

In the transverse sinuses the contrast medium may collect in one or both margins during emptying If the inflow effect from a venous branch is added

the picture would theoretically resemble a thrombosis (We have not so far seen a thrombosis)

All pathologic findings should be judged with reserve and confirmation should be sought by means of an injection in a different position Fig 12 shows a filling defect in the anterior wall of the vein it is probably an artefact caused by the inflow from the common facial vein If there had been reason to suspect a tumour in this region it would have been necessary to re examine the patient in the prone position with the catheter further down

ZUSAMMENFASSUNG

Eine eingehende Beschreibung der Technik der retrograden Jugularographie und der normalen Variationen der Sinus transversus und Vena jugularis interna wird gegeben Der Wert dieser Methode fur die Untersuchung der Drainierung des Hirns vor Drusenausraumung wird erörtet Die Variationen des Bulbus vena jugularis interna werden beschrieben Der Wert von der Methode fur die Diagnostik von Tumoren in und um Foramen jugulare wird hervorgehoben

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Dept of Oto rhino laryngology
Karolinska sjukhuset Stockholm 60
Sweden

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ATTEMPT OF DETERMINING THE FETAL REACTION TO ACOUSTIC STIMULATION

B Dwornicka, A Jasienska, W Smolarz and R Wawryk
Zabrze, Poland

From the Ear, Nose and Throat Clinic (Head Prof T Ceypek), the Clinic of Internal Diseases (Head Prof W Zahorski) and the Clinic of Gynecology and Obst (Head Prof W Starzewski), The Silesian Medical Academy, Zabrze

The authors examined reaction of rhythm of the fetus heart in 32 pregnant women in the last month of pregnancy, after tone giving of 1000 and 2000 c/s and of intensity 100 db for 5 sec The pulses of the mother and fetus were registered by Hellige s phonocardiograph before, during and after tone giving

Acceleration of fetus heart was observed in the group tested 1000 c/s average 7 beats a minute in the group tested 2000 c/s 11 beats a minute The mother s pulse did not show any acceleration during the tone or later on

The interest in the physiology of the hearing sense in human fetuses is comparatively little Preyer in 1885 stated with almost certainty that infants before their birth have no developed sense of hearing Peiper in 1925 had noticed some fetal movements on acoustic stimulations caused by automobile horn

The development of audiometry made possible an exact examination by calibrated acoustic stimulations Sontag and Wallace, and Sontag and Richards recorded intrauterine fetal movements and cardio accelerations of the fetus after applying a vibratory stimulus of 120 c/s

Similar examinations were performed in 1955 by Fleischer who registered graphically the movements of fetuses over six months old after tone giving Under the theoretical considerations of the author he states that the membranous labyrinth is the earliest fully shaped part of the temporal bone, and the auditory nerve is the earliest one of all nerves, covered with sheath According to Bleischmidt a primitive receiving of sound stimulations by the Corti organ is possible This is confirmed by the reactions of premature babies to the acoustic stimulations in form of accelerated respirations increased movements and aural palpebral responses

The easiest measurable reaction of the auditory stimulations is the rhythm of the fetus heart Therefore the Bernard s & Sontag s observation (1947) appeared to us to be most conclusive

The authors observed in 5 cases the response of the fetus pulse examined by means of the Brush s apparatus applied on the place of the best ausculta tion of its pulse The tone was given with an audiometre through the micro

phone applied above the symphisis pubis over the infant's head. The examinations of whole tone scale below 6000 c/s were performed. The tone was given for 5 seconds and just after acceleration averaging 5 beats a minute was obtained. We examined this phenomenon with improved technical methods and with a wider material than observed by Bernard and Sontag.

METHOD AND RESULTS

32 pregnant women in the last month of pregnancy were examined. By means of anamnesis were excluded cases of deafness in the family, with syphilis, alcoholism, diseases endured during pregnancy and taking drugs acting upon the auditory organ.

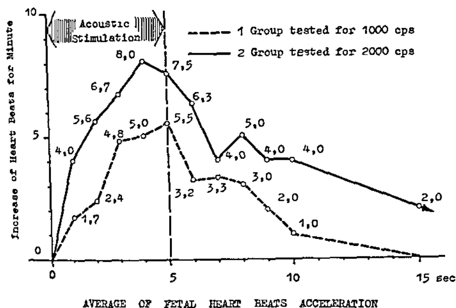
The examinations were performed in the following way. A pregnant woman was examined in lying still position in a room in which the level of noise intensity was 35 db measured by Bruel and Kjaer sonometre. For registration of the pulse a three canal Hellige's phonocardiograph was used allowing a direct evaluation of the record. With the first canal the electrocardiograph of the mother was registered, and with the second and third one the fetus's pulse with filters m_1 and m_2.

The action of the heart was registered before, during and after giving the tone, till the moment the action of the heart came back to the starting frequency. The tone was given with an audiometre constructed at the Polytechnical School in Gliwice through the earphone enclosed in a rubber cuff placed above the symphysis pubis in the region of the infant's head. The intensity of the tone was 100 db. The response to the tone of 1000 and 2000 c/s was examined. The tone was given for 5 seconds. The resgistration of the fetus' pulse and its measurement for some time before giving the tone allowed to establish that the physiological oscillations of the fetus pulse were slight.

The material was divided into two groups. The first group of 11 cases was examined with the tone of 1000 c/s and of intensity of 100 db. At the time of giving the tone or just after it, the rate of the heart action of fetus rapidly increased 3 to 13 beats a minute (on average 7) as compared with the mean frequency before giving the tone. The heart action of the fetus returned to a normal state between the 5th to 15th second. The simultaneous registration of the mother's pulse in the time of the whole examination did not show any acceleration during giving the tone or later on.

The other group counting 21 cases was examined under the same conditions but with the tone of frequency of 2000 c/s. In this group a remarkably higher acceleration of 4 to 29 beats pulse underwent an acceleration in the course of giving the tone.

In 2 cases a contrary reaction was found; just after the tone had been given a deceleration of the heart action occurred, in one fetus 10 beats a minute, in the other one 5 beats a minute. In one case no alteration of the pulse after the tone had been given was obtained. This child was examined in the fourth



AVERAGE OF FETAL HEART BEATS ACCELERATION

Fig 1

week after birth but no reliable results were obtained We shall go on observing this case

In order to exclude any possibility of influences of external stimulations as e g touching after applying the stethoscope or others 30 pregnant persons were examined as the control group in identical conditions of examination but without tonal stimulus No pulse acceleration of the fetus was found in the control group

In some cases chosen by allotment from the examined with 2000 c/s the tone of the same frequency was given again immediately after the first examination was finished Then no reaction was observed After a 10 minutes break the reaction ran in a typical way

DISCUSSION

The method of our examinations fundamentally resembling that of Bernard and Sontag is however different from it as we made use of more precise apparatus allowing to register simultaneously the pulse of the mother and fetus and recording the heart action also in the time of tone giving Owing to this it was possible to state that the mother showed no emotional reaction involved in the vibratory stimulation that would be made perceivable by a cardiac acceleration Therefore it may be assumed with great probability that the stimulations transmitted by the mother have no influence upon the reaction of acceleration in the fetus Bernard and Sontag had no possibility of observing the behaviour of the fetus pulse at the time of tone giving and obtained the first measurement after stopping the tone i e in the 6th second

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The examinations were performed in the following way. A pregnant woman was examined in lying, still position in a room, in which the level of noise intensity was 55 db, measured by Bruel and Kjaer sonometre. For registration of the pulse a three-canal Hellige's phonocardiograph was used allowing a direct evaluation of the record. With the first canal the electrocardiograph of the mother was registered, and with the second and third one the fetus's pulse with filters m_1 and m_2.

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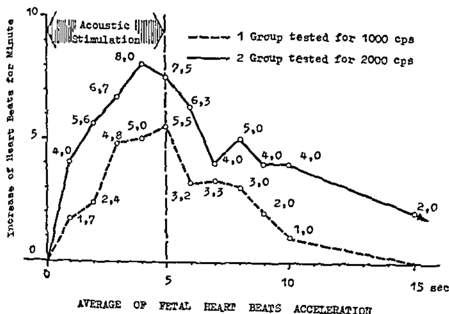


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The examinations were performed in the following way. A pregnant woman was examined in lying still position in a room in which the level of noise intensity was 55 db measured by Bruel and Kjaer sonometre. For registration of the pulse a three canal Hellige's phonocardiograph was used allowing a direct evaluation of the record. With the first canal the electrocardiograph of the mother was registered and with the second and third one the fetus's pulse with filters m_1 and m_2.

The action of the heart was registered before, during and after giving the tone till the moment the action of the heart came back to the starting frequency. The tone was given with an audiometre constructed at the Polytechnical School in Gliwice through the earphone enclosed in a rubber cuff placed above the symphysis pubis in the region of the infant's head. The intensity of the tone was 100 db. The response to the tone of 1000 and 2000 c/s was examined. The tone was given for 5 seconds. The registration of the fetus' pulse and its measurement for some time before giving the tone allowed to establish that the physiological oscillations of the fetus pulse were slight.

The material was divided into two groups. The first group of 11 cases was examined with the tone of 1000 c/s and of intensity of 100 db. At the time of giving the tone or just after it the rate of the heart action of fetus rapidly increased 5 to 13 beats a minute (on average 7) as compared with the mean frequency before giving the tone. The heart action of the fetus returned to a normal state between the 5th to 15th second. The simultaneous registration of the mother's pulse in the time of the whole examination did not show any acceleration during giving the tone or later on.

The other group counting 21 cases was examined under the same conditions but with the tone of frequency of 2000 c/s. In this group a remarkably higher acceleration of 4 to 29 beats pulse underwent an acceleration in the course of giving the tone.

In 2 cases a contrary reaction was found just after the tone had been given a deceleration of the heart action occurred, in one fetus 10 beats a minute, in the other one 5 beats a minute. In one case no alteration of the pulse after the tone had been given was obtained. This child was examined in the fourth

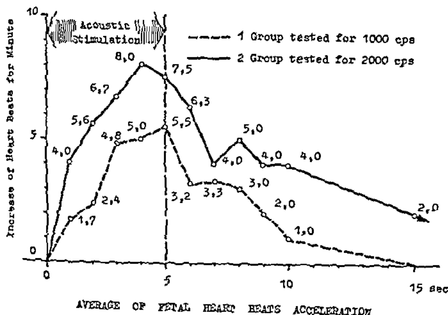


Fig 1

week after birth but no reliable results were obtained We *shall go on* observing this case

In order to exclude any possibility of influences of external stimulations as *e g touching* after applying the stethoscope or others 30 pregnant persons were examined as the control group in identical conditions of examination but without tonal stimulus No pulse acceleration of the fetus was *found in* the control group

In some cases chosen by allotment from the examined with 2000 c/s the tone *of the same* frequency was given again immediately after the first examination was *finished* Then no reaction was observed After a 10 minutes break the *reaction* ran in a typical way

DISCUSSION

The method *of our* examinations fundamentally resembling that of Bernard and Sontag is however different from it as we made use of more precise *apparatus allowing* to register simultaneously the pulse of the mother and fetus and *recording* the heart action also in the time of tone giving Owing to this it was *possible to state* that the mother showed no emotional reaction involved *in the vibratory* stimulation that would be made perceivable by a cardio acceleration Therefore *it may* be assumed with great probability that the stimulations *transmitted by* the mother have no influence upon the reaction of *acceleration in the fetus* Bernard and Sontag had no possibility of observing the behaviour of the fetus pulse at the time of tone giving and obtained the first *measurement after* stopping the tone i e in the 6th second

On watching the continuous record of the heart action at the time of tone giving we could find out that in some cases it came to the highest acceleration of the action as early as in the first second of tone giving, and the heart action became normal again many times in the 5th second.

The temporal connection of the pulse acceleration during tone giving would point to a doubtless association with the action of the acoustical stimulation. The rate of this reaction excludes the possibility for the stimulation to be transmitted by the mother on the way of blood through the placenta.

The above work constitutes the introduction to the studies projected by us on the early detecting of deafness in infants.

ZUSAMMENFASSUNG

Man hat die Reaktion der Fötusse auf akustische Reize bei 32 schwangeren Frauen in den letzten Monaten der Schwangerschaft untersucht. Während der Untersuchung wurden die Pulsfrequenzen der Fötusse und der Mutter registriert. Als Reiz wurden Töne von 1000 und 2000 Hz, mit der Intensität von 100 Decibel, verwendet.

Die Pulsfrequenzen der Mutter und der Fötusse wurden gleichzeitig vor, während und nach der Tonapplikation registriert. Die Pulsfrequenz wurde bei 1000 Hz durchschnittlich um 7 Schläge und bei 2000 Hz um 11 Schläge auf 1 Minute beschleunigt. Die Pulsreaktion der Mutter änderte sich nicht.

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B. Dwornicka and A. Jasieńska, E.N.T. Clinic
Silesian Medical Academy
Curie Skłodowskiej 10, Zabrze, Poland

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GENERAL OROTRACHEAL ANESTHESIA FOR BRONCHOSCOPY

J KORKEILA and T PALVA
Turku Finland

From the Departments of Anesthesia and Otolaryngology, University of Turku

Bronchoscopy was made under general orotracheal anesthesia by introducing into the trachea a cuffed No 4 or 5 Magill endotracheal tube followed by the bronchoscope Intermittent positive pressure respiration with nitrous oxide and oxygen was used The technique ensured good operating conditions without time limit PCO_2 in arterialized capillary blood was analysed in seven patients during the procedure in some samples there was a minor rise in CO_2 tension

Bronchoscopy under general anesthesia presents certain practical problems because of the necessity for both the anesthetist and the bronchologist to work in the airways In these examinations the patient is allowed either to breathe spontaneously or is relaxed completely by means of muscle relaxants In the latter method the patient is given a continuous flow of oxygen or intermittent positive pressure respiration (IPPR) is maintained through the side arm of the bronchoscope Some centers leave the bronchologist to work alone in the airways while the anesthetist effects the patient s ventilation with an external cuirass type respirator

Reitman (1957) described a modified endotracheal technique for general anesthesia in bronchoscopy This method consisted of introduction into the trachea of both the intubation tube and the bronchoscope A closely similar method was adopted by Lammert (1961) Rogers & Erhardt (1961) and by Pang (1962) with encouraging results Because the technique seemed to be simple and to offer certain advantages over other techniques we have used it in a somewhat modified form for diagnostic bronchoscopy Our experience with this method from a period exceeding one year will be reported below

MATERIAL AND METHOD

The material comprises 63 patients 58 male and 5 female ages varying between 11 and 70 years A gross impairment of respiratory function was diagnosed in one fifth of the patients with the aid of respiratory function tests blood gas analysis or clinically In 13 cases bronchoscopy was performed as a preliminary step to mediastinoscopy, the anesthesia being continued by the usual method after termination of bronchoscopy

Premedication consisted of pethidine 50 mg and atropine 0 5 mg given intramuscularly one hour before the procedure On the operation table the

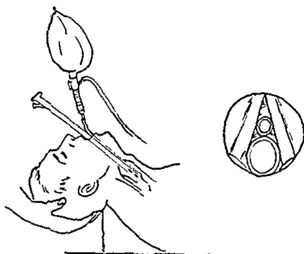


Fig 1

patient was allowed to breathe 100 per cent oxygen for five minutes During this time 100 mg of lidocaine (Xylocaine®) was given intravenously (10 ml of 1 per cent solution) 200 to 400 mg of thiopentone was then administered followed by succinylcholine 50 to 100 mg The patient was ventilated with oxygen for a short period and a No 4 or 5 well lubricated cuffed Magill endotracheal tube was passed into the trachea The anesthetist or bronchologist introduced the bronchoscope through the laryngeal aperture (Fig 1) In most cases the intubation tube lied in the anterior commissure but sometimes it was easier to place the bronchoscope anteriorly The cuff of the Magill tube was filled with air but the tube was not fixed in position It was then connected to a to and fro system of the anesthetic machine A flow of 5 litres of oxygen and 10 litres of nitrous oxide per minute was used The patient was ventilated in the usual manner and relaxation was achieved by 0 2 per cent succinylcholine drip It was very easy to ventilate the patient even when the proximal

TABLE 1 *PCO_2 (mm Hg) in arterialized capillary blood*

Case No	Before anesthesia	During anesthesia 5 min	10 min	15 min	Comments
1	51	52	50	42	Compensated resp acidosis
2	41	42	43		
3	49	50	[illegible]		
4	55	57	57	8	Compensated resp acidosis
5	44	47	45		
6	39	42	37		
7	39	45	[illegible]		Vital cap [illegible] % of normal Sec cap 15 %/1 s

end of the bronchoscope was open Examination of the bronchial tree could be performed without difficulty and there was no time limit The duration of the bronchoscopic examination varied in this series from 5 to 22 minutes

During the initial period of anesthesia there was a tendency for the blood pressure to rise apparently owing to succinylcholine and the light level of anesthesia

An analysis was made of the PCO_2 in arterialized capillary blood using the micro Astrup technique (Siggaard Andersen *et al*, 1960) and the results are presented in Table 1 There was a negligible rise of the PCO_2 in some samples The proximal end of the bronchoscope was left open for about half of the time needed for the procedure

After bronchoscopy the patients regained consciousness quickly and were able to cough up sputum and blood from the airways Since the adoption of intravenous lidocaine we have not seen any cases of vigorous coughing or laryngospasm which were sometimes troublesome without this medication

DISCUSSION

Bronchoscopy under local analgesia sometimes causes great discomfort to the patient and the operator cannot perform all phases of the examination as thoroughly as he would like In certain rare cases with a very short and stiff neck even the introduction of the bronchoscope into the trachea is unsuccessful with this technique

Local analgesia supplemeted with intravenous pethidine gives better and more comfortable conditions for the procedure (Knudsen *et al* 1958) and practically no difficulties are encountered in adequate general anesthesia

It has been claimed that local anesthetic drugs like tetracaine and to some extent even lidocaine have an inhibitory effect on the cultural growth of fungi and of nontuberculous bacteria (Erlich 1961) and even of Myco bacterium tuberculosis (Conte & Laforet 1962) However it is difficult to say definitely how much clinical significance can be attributed to this finding

Several methods are used for bronchoscopy under general anesthesia The patient can be anesthetized with intravenous barbiturate and relaxed with short acting muscle relaxant Bronchoscopy carried out during apnoea is suitable for very short procedures only The insufflation method with an oxygen catheter in the carina is also recommended for quite short examinations (Ruben & Rasmussen 1956) When the ADO (apnoeic diffusion oxygenation or apnoeic mass movement respiration) technique (Holmdahl 1953 Barth 1954 Riecker 1955) is used adequate oxygenation can be maintained but there is a continuous rise of arterial blood PCO_2 of the order of 6 mm Hg per minute (Mundnich & Zulke 1956 Holmdahl 1956 and 1961) This technique can maintain oxygenation of the patient during periods when the bronchoscope is open and controlled ventilation with pure oxygen through a side arm of the bronchoscope is impossible If the ADO method is used with THAM (Tris buffer) it is possible to keep the PCO_2 level fairly constant

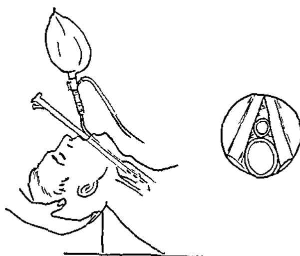


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5	41	47	45		
6	39	42	37		
7	39	45	47		Vital cap 49 % of normal Sec cap 45 %/1 s

ZUSAMMENFASSUNG

Die Bronchoskopien wurden unter orotrachealer Allgemeinanasthesie durchgefuhrt Es wurde zunachst ein Magillendorachealtubus No 4 oder 5 eingefuhrt, danach das Bronchoskop Es wurde intermittierende Uberdruckbeatmung mit Lachgas/Sauerstoff benutzt Diese Methode gewahrleistete gute Operationsbedingungen ohne zeitliche Begrenzung PCO_2 im arterialisierten Kapillarblut wurde bei 7 Patienten wahrend des Eingriffs untersucht Bei einigen Proben war ein geringer Anstieg der CO_2 Spannung

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without IPPR as shown by Holmdahl (1961) The apnoeic oxygenation technique is also used with halothane for direct laryngoscopy and according to Payne (1963) the CO_2 tensions could rise to a very high level without any apparent harm to the patient

A bronchoscope made airtight with a shortened Magill endotracheal tube surrounding the proximal part of the instrument (Churchill Davidson 1953) or a special ventilation bronchoscope (i e Konig 1956) can be used for *intermittent positive pressure respiration* It is not possible however to ventilate the patient when the proximal end of the bronchoscope is open

A completely relaxed patient can also be ventilated by compressing the thorax manually or with the aid of a special belt (Pinkerton 1957) or with a curass type of respirator (Green & Coleman 1955) The thoracic compression can hardly produce effective ventilation in every case even when used for assisted respiration and the cuirass respirator is inapplicable in patients having a large loose abdomen or a short rigid thorax or emphysema (Ruben & Rasmussen)

When letting the patient breathe spontaneously a deep level of general anesthesia is needed Therefore it is more practical to combine light general anesthesia with topical analgesia and to give subparalysing doses of muscle relaxants if necessary Various anesthetic agents can be used in the original *technique of Reitman nitrous oxide was employed However halothane* seems more suitable for this technique It can be given through a catheter at the bifurcation as described by Boulton (1963) Forl e *et al* (1962) analysed the arterial PCO_2 during bronchoscopy when the patient was breathing spontaneously There was frequently a 100 per cent increase in the arterial PCO_2 when muscle relaxants were used

The method described by us seems to give good operating conditions It is simple and there is no need for special instruments or drugs The patient *can be ventilated adequately without any time limit and fairly effectively* even if the proximal end of the bronchoscope is open Consciousness is regained quickly and the patient is able to cough up mucus and blood from the airways Wyant (1963) commenting on the paper of Rogers & Erhardt says that of all the methods advocated for bronchoscopy under general anesthesia this surely must be among the least desirable Our experience is not in agreement with this opinion The excellent effect of intravenous lidocaine in depressing the pharyngeal and laryngeal reflexes as reported by Steinhaus & Howland (1958) and by Holmdahl (1962) was confirmed by our study

In our experience this technique should be limited to adult patients In children the size of the *larynx does not easily accommodate separate tubes* and a forceful introduction only results in laryngeal oedema Other fields in which orotracheal anesthesia with a small endotracheal tube has provided excellent working conditions are direct laryngoscopy *and the removal of* various benign laryngeal tumors This has also been shown by Sachs (1962) in a series of 90 cases

ZUSAMMENFASSUNG

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Dept. of Anesthesia and Otolaryngology
University of Turku, Finland

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SITE OF ACTION OF STREPTOMYCIN UPON INNER EAR SENSORY CELLS

ARNDT J DUVALL[1] and JAN WERSALL
Stockholm Sweden

From the Department of Otolaryngology (Head Prof C A Hamberger) Karolinska Sjukhuset, and the King Gustav V Research Institute (Head Prof G Birke) Stockholm 60

The effects of streptomycin on the inner ear sensory epithelia were studied in guinea pigs by means of the electron microscope The most severe damage was found in the vestibular sensory cells starting with degeneration of and myelin figure formation in the mitochondria Later swelling appeared in the sensory hairs with deformation of the cell surface, and finally disappearance of the sensory hairs swelling of the cell surface often with rupture and ejection of cells and cell debris into the endolymph Nerve fibers and nerve endings were unchanged The organ of Corti was less extensively damaged Changes were confined to the mitochondria and stereocilia of the hair cells The damage of the sensory cells was explained as an affection mainly of the plasma membrane of the cell and the membrane component of the mitochondria with inhibition of the formation of the rigid component of the membranes and damage to the permeability barrier

The ototoxic action of streptomycin and its derivates has been well documented through clinical as well as experimental studies since it was first found in humans (Hinshaw & Feldman 1945) and reproduced in dogs (Molitor *et al* 1946) The literature in this field has been reviewed lately by Wersall & Hawkins (1962) and Tyberghein (1962) Although nerve cell damage has been described in the vestibular ganglia (Floberg Hamberger & Hyden 1949) and in the brain (Christensen *et al* 1950) the predominating changes are found in the vestibular epithelia (Berg 1951 Hawkins & Lurie 1952) By means of the electron microscope Wersall & Hawkins (1962) demonstrated a relatively selective effect on the sensory cells in the vestibular apparatus compared to the supporting cells suggesting a specifically high degree of sensitivity in the sensory cells

Several studies have been undertaken on the effect of streptomycin on connective tissue cells and muscle cells in tissue culture and Friedman & Bird (1961) followed progressive changes in mitochondria in isolated fowl embryo oocysts after treatment with various antibiotics However the exact

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[1] Visiting NIH Special Fellow from the University of Minnesota

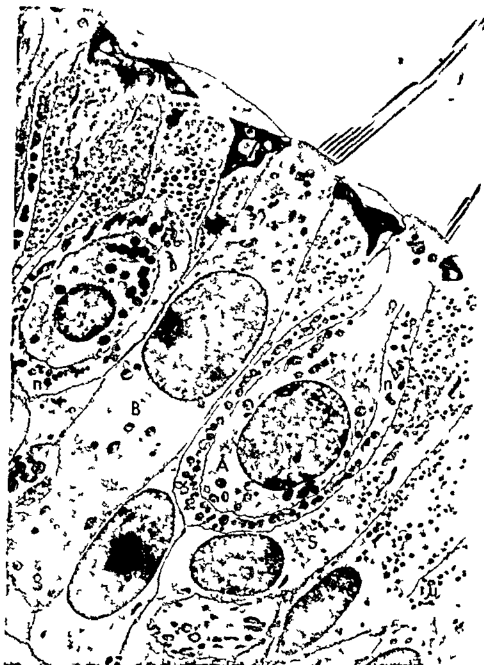


Fig. 1. Normal lateral ampulla neuroepithelium. Type I (*A*) and type II (*B*) hair cells. Supporting cell (S). Nerve chalice (N). ×5000

site of action of streptomycin on bacteria, as well as other cells, has not been established. We found the sensory cells in the inner ear, with their relatively high sensitivity for the toxic action of streptomycin, were an excellent cell type for studies of antibiotic action. The present work was done in order to study the early stages of damage in the sensory cells of the inner ear.

MATERIAL AND METHODS

Thirty young guinea pigs weighing between 190 and 310 grams and without evidence of otitis media were used for the experiment. Six of these



F g 2 *Lateral ampulla neuroep thel um of guinea p g tha* ... 200 —

animals were controls and were given saline injections Twenty four received 300 mg of streptomycin sulfate per kilogram per day I M in the back divided into two doses All the animals lost between 15 and 20 per cent of their original weight the first week Seven of these animals died between the seventh and tenth day The remaining seventeen quickly recovered their weight and healthy appearance The animals were divided into four groups in regard to dosage being given streptomycin for 8 15 20 and 35 days

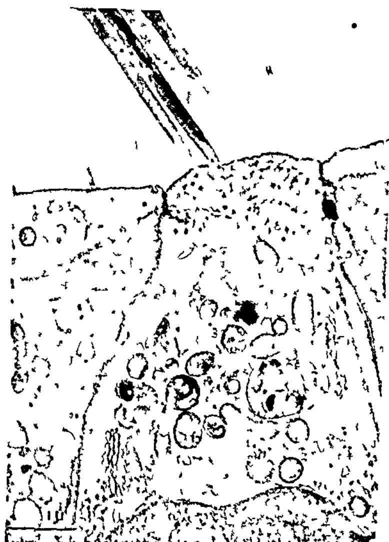


FIG. 3. Type II hair cell in lateral ampulla of streptomycin intoxicated guinea pig. Supranuclear mitochondrial changes with intact cilia. Note early indentation of nucleus. ×22 000

TABLE 1

Guinea pig	Days of streptomycin (300 mg/kg/day)	Day of sacrifice	Pinna reflex at sacrifice	Calorics at sacrifice
D 5	8	11		Normal
D 29 D 31	15	15		0
D 18 D [illegible]	15	19		0
D 20 D [illegible]7	15	30		
D 31	15	10		[illegible]
D 32	15	61		
D 23 + D 24	20	21		0
D 9 + D 10	20	27		[illegible]
D 19 + D [illegible]2	[illegible]	30	+	0
D 28	[illegible]	50		0
D 11	3	[illegible]	+	[illegible]



Fig. 4. Ampulla after streptomycin treatment. The type I cell (left) protrudes its entire supranuclear portion. It is devoid of cilia. The type II hair cell (right) demonstrates a typical giant cilium. Note the mitochondrial changes and the cleft nucleus containing mitochondria. × 13,000.

respectively. They were allowed to survive for varying lengths of time as shown in Table 1.

Vestibular function was followed by rotatory testing and observation of the righting reflexes. By the 15th day of streptomycin, all animals had impaired righting reflexes and no post-rotatory nystagmus. D 11 was an exception, as its vestibular function did not cease until the 36th day. No recovery of function was noted in any animal. D 5, which received 8 days of streptomycin, demonstrated normal vestibular function at sacrifice on the 14th day. 10 cc ice water calorics were performed under direct observation with the Zeiss operating microscope on the day of sacrifice. With the exception of D 5, no animal demonstrated nystagmus.

A good Preyer reflex was a prerequisite for animal selection and was maintained in all animals throughout the experiment. In a few guinea pigs the cochlear microphonics were measured via the round window just before

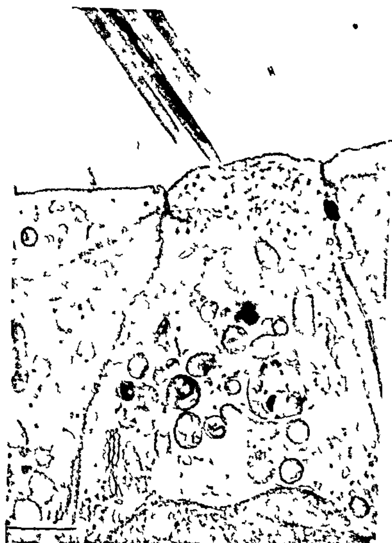


FIG. 3. Type II hair cell in lateral ampulla of streptomycin intoxicated guinea pig. Supranuclear mitochondrial changes with intact cell. Note early indentation of nucleus. ×22 0 0

TABLE 1

Guinea pig	Days of streptomycin (300 mg/kg/day)	Day of sacrifice	Lima reflex at sacrifice	Calorics at sacrifice
D 5	8	14		Normal
D 29 D 34	15	15		0
D 18 D 25	15	19		[illegible]
D 20 D 27	15	3[illegible]		[illegible]
D 31	15	40		
D 32	15	[illegible]		[illegible]
D 23 + D 24	20	21		[illegible]
D 9 + D 10	[illegible]	2[illegible]		[illegible]
D 19 + D 22	[illegible]0	30		0
D 28	[illegible]	[illegible]0		0
D 11	3[illegible]	[illegible]		0

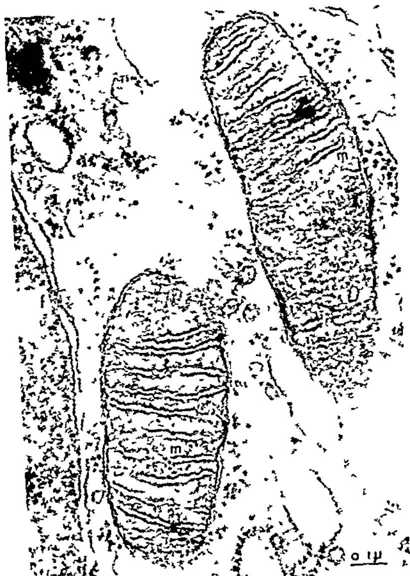


Fig 6 Morphologically normal supranuclear mitochondria (M) in severely damaged type I vestibular hair cell Note fenestra (f) in normal nuclear membrane × 140 000

and no impairment of nystagmus reaction as studied with our methods In all the other animals the same type of damage was found in the inner ear sensory epithelia The variation in degree of damage was relatively small between animals and correlated poorly with total dosage and length of time between cessation of streptomycin injections and sacrifice

Vestibular Sensory Epithelium

The major damage was found in the vestibular end organs of the ampullae and the utricle The saccule was not studied in this experiment No dif

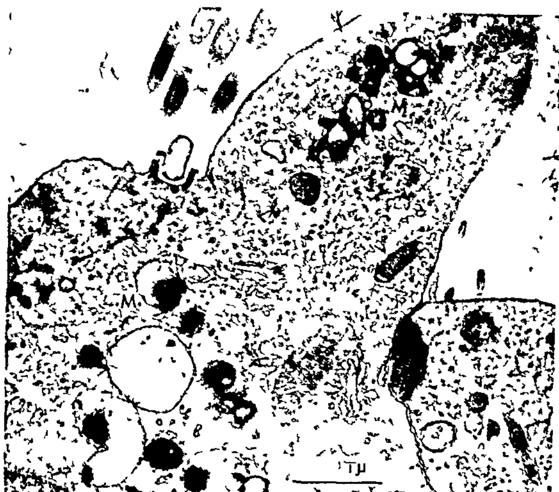


Fig. 5. Top of type I hair cell in ampulla of streptomycin treated guinea pig. Stereocilia are swollen, mitochondria (M) degenerate and cytoplasm bulging into the lumen. × 30 000.

sacrifice. Each gave excellent responses at all frequencies between 500 and 4000 cps.

The animals were sacrificed in room temperature. This was followed by rapid dissection of the temporal bones, exposure of the cochlear apex, opening of the round and oval windows and exposure of the semicircular canals to allow good penetration of the fixative: 1 % buffered isotonic osmium tetroxide solution (Rhodin 1954). After three hours fixation the specimens were rinsed in Ringer's solution and dissected in 70 % alcohol with separation of the ampullae and utricle from the rest of the specimen. The specimens were imbedded in Epon, sections cut on an LKB Ultratome, stained with a saturated solution of uranyl acetate for 60 minutes at 70°C (Brody 1959) and photographed in a Siemens Elmiskop I electron microscope at initial magnifications of × 1800 to 40 000.

RESULTS

No definite changes were found in the structure of the vestibular sensory epithelia and organ of Corti in the guinea pigs given streptomycin for 8 days, or in the controls (Fig. 1). These animals had normal righting reflexes

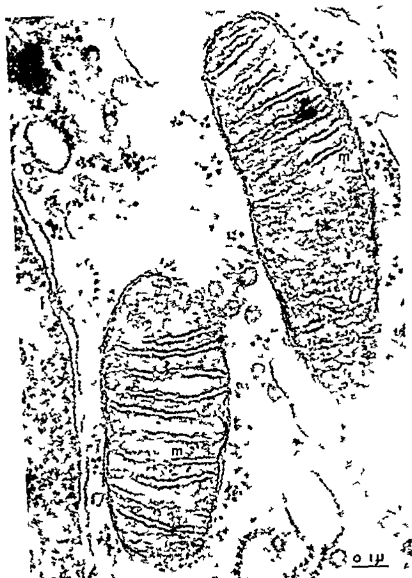


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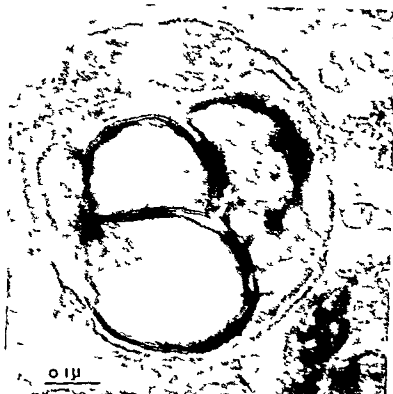


Fig. 7. High magnification of damaged mitochondrion. Type I vestibular hair cell. Internal membrane system is destroyed and concentric lamellae are forming. × 180 000

ference in degree of damage was found between the utricle and the ampullae. The changes engaged predominantly the hair cells of the sensory areas and were found equally distributed over all the sensory areas in both type I and type II hair cells. The variation in degree of damage to individual sensory cells within any one specimen was relatively large, thus enabling us to document the course of cell destruction.

The first morphological sign of damage was observed in the mitochondria of the supranuclear part of the cell, that is, toward the hair bearing end. Some of the mitochondria showed disintegration of the internal membranes, formation of dark irregular granules between the two layers of the internal membranes and replacement of the membranes with lamellae of the myelin figure type (Figs. 2, 3, 4, 5). Myelin figures were first found as irregular lamellae within the mitochondria. Later several concentric lamellae appeared filling a good part of a mitochondrium, often forming quite regular figures of alternating osmophilic and osmophobic bands 23 Å in diameter (Fig. 7). During these changes many mitochondria were found to swell to bodies several times the normal size. The outer double membrane often gave way to a single layer. In the final stage of changes the mitochondria appeared as swollen vesicles containing varying amounts of amorphous osmophilic substance with or without myelin figures.

Changes did not strike all mitochondria in the cells at the same time, for



Fig 8 Superior portion of streptomycin damaged internal hair cell Mitochondrial changes are typically confined to supranuclear area but do not extend to mitochondria immediately subjacent to the cuticle Nucleus (N) Cuticle (C) Inner pillar (I) × 12 600

well preserved mitochondria could be observed even in extensively damaged cells (Fig 6) The Golgi apparatus appeared unchanged but occasional dilatations of endoplasmic reticulum were observed Irregular contours often appeared in the superior surface of the sensory cell nuclei occasionally as deep clefts containing mitochondria However, we were unable to find morphological breakdown of the nuclear membrane (Fig 6)



FIG. 9. Supranuclear area streptomycin damaged internal hair cell. This illustrates the wide range of mitochondrial changes. × 30 000

Surface Membrane

The stereocilia were found to swell and sometimes giant cilia of tremendous diameters were observed. Some of the cilia appeared to merge as if the surface membrane between them had disappeared. Even the surface membrane of the cell and the cuticle are changed in such a way that the stereocilia and the kinocilia disappear, and the supranuclear portion of cell bulges out into the endolymphatic space. Mitochondria in various stages of degeneration, as well as other cell organelles, are



I 10 H gh magn ficat on of supranuclear m tochon ir um of internal hair cell n streptomyc n intoxicat on Normal internal membrane system de troyed Mo lerately well organized myel n f gu e 13) 000



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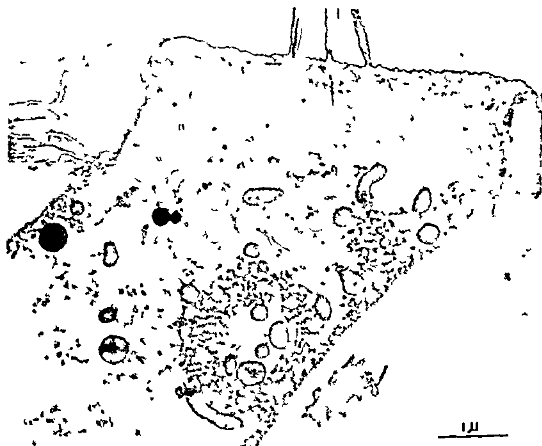


Fig. 12. Normal superior portion of cochlear outer hair cell in a control animal. Cut perpendicular to basilar membrane. × 21 000.

jections. Some cells are completely pushed out into the lumen of the endolymphatic space whereas others lose their surface membrane with all hairs and part of the cytoplasm. We have found no tendency of the cell to rebuild the plasma membrane, for the cell remains open towards the endolymph with a ragged upper surface.

Nerve Endings

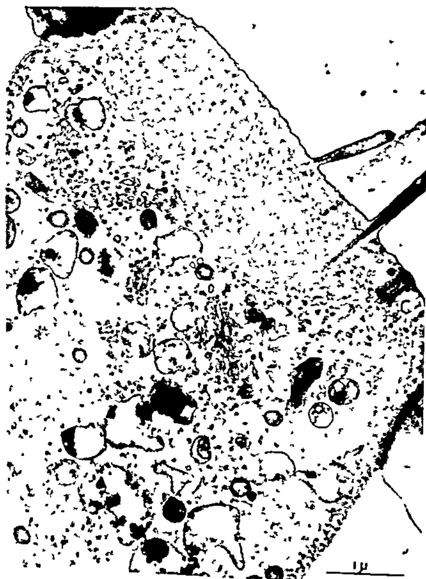
Only occasionally were any abnormalities found in the mitochondria of the infranuclear part of the cell. The nerve endings, as well as the nerve fibers and their myelin sheaths, and Schwann cells in the subepithelial area were unchanged.

Supporting Cells

An increased number of lipid granules were found in the supporting cells, but there were no changes in the surface membrane, granules or mitochondria. All secretory areas were found normal as described by Kimura *et al.* (1963).

Cochlear Findings

The sensory cells and the supporting cells, as well as the nerve endings and nerve fibers, were studied by sections parallel to, as well as perpendi-



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cular to the basilar membrane The organ of Corti was better preserved than the vestibular sensory areas The morphological changes were confined to the sensory hairs and the mitochondria of the supranuclear part of the hair cells (Figs 8, 9 10, 11 13)

Thus some of the hairs in both internal and external sensory cells were found to be swollen up to two times normal diameter All hairs were, however, found to be preserved and normal in form The most pronounced changes



FIG. 14. Cochlear hair cells in control animal. Section is parallel to basilar membrane directly under cuticle. × 12 600.

were in the mitochondria of the supranuclear part of the cell. These mitochondria showed the same type of changes as their brothers in the vestibular hair cells. They were swollen with disintegrated internal mitochondrial membranes, and more or less filled with dark inclusions and myelin figures (Figs. 4, 5, 8). As in the vestibular sensory cells, not all the mitochondria showed changes.

We found no morphological difference in degree of early streptomycin intoxication in different parts of the cochlea. Neither was there a difference in various rows of outer hair cells or between inner and outer hair cells.



Fig. 1. Outer hair cells showing extensive mitochondrial damage. Section as in Fig. 15. × 13 000.

DISCUSSION

The morphological findings in the above material are in agreement with the physiological findings. As the displacement of the sensory hairs is looked upon as the adequate stimulus for the cells, no response from the vestibular sense organs could be expected when most of the vestibular cells had severely damaged hair bearing ends. Although mitochondrial changes in the vestibular sensory cells were universal, the hairs and cuticles of occasional cells appeared normal. If these cells remained functional, they were apparently of insufficient number for our crude functional tests to discern.



Fig. 14. Cochlear hair cells in control animal. Section is parallel to basilar membrane directly under cuticle. × 12 600.

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Fig. 15. Outer hair cells showing extensive mitochondrial damage. Section as in Fig. 15. 13 000

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as claimed by Landman *et al.*, be explained by the fact that these enzymes in most bacteria are connected to the surface membrane.

As stated by Friedman & Bird (1961) and Wersall & Hawkins (1962) predilection for the sensory cells of the inner ear seems to show that there is a specific concentration of streptomycin in the inner ear.

ACKNOWLEDGEMENT

The authors are indebted to Miss Ann Marie Lundberg, Dr P. G. Lundquist, Mr G. Bornholm for their technical assistance and to KABI who kindly supplied the streptomycin sulfate used in this study.

ZUSAMMENFASSUNG

Die Effekte von Streptomycin auf die Epithele des inneren Ohrs des Meerschweinchens wurden mit dem Elektronenmikroskop studiert. Der grösste Schaden wurde in den vestibulären Sinneszellen beobachtet, anfangend mit Degeneration der Mitochondria und Myelinfigurformation in ihnen. Später erschienen ein Anschwellen von Sinneshaaren mit Deformation der Zellenoberfläche, schliessliches Verschwinden der Sinneshaare, Anschwellen der Zellenoberfläche, oft mit Zerreissung und Auswurf von Zellen und Zellendébris ins Endolymph. Nervenfasern und Nervenenden blieben unverändert. Das Cortische Organ war weniger beschädigt. Veränderungen waren auf die Mitochondria und Stereocilia der Haarzellen beschränkt. Der Schaden von Sinneszellen wurde erklärt als eine Affektion hauptsächlich der Plasmamembrane der Zelle und der Membranenkomponente der Mitochondria mit Inhibition in der Bildung der rigiden Membranenkomponente und Beschädigung der Permeabilitätsbarriere.

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The normal Preyer reflex and/or good cochlear microphonics in all animals would indicate that the changes in the cochlear hair cells were not severe enough to destroy the hearing although some impairment might have appeared without being observed with our tests. It appears then that some degeneration might occur in the mitochondria without complete *destruction of cell function* provided the sensory hairs and some of the mitochondria are normal or little changed.

The actual site of action of *streptomycin and other antibiotics* has been the subject of intensive study by many workers. Our findings on the mitochondria of guinea pig inner ear sensory cells are in agreement with those of Friedmann & Bird (1961) on isolated fowl otocysts. These authors stressed the importance of the mitochondria as carriers of enzymes essential for cell metabolism but did not discuss the effect of streptomycin on the surface membrane.

Although our study would indicate that the earliest changes are in the membrane system of the mitochondria extensive morphological changes occur at the cell surface. In an attempt to assign a unitary cause for these multiple effects we would like to focus on the membrane system.

Weidel, Frank & Martin (1961) have shown that loss of rigidity of *E. Coli* is due to depolymerization of the mucopeptide chains linking together amino acid containing spherical elements in the innermost of the 3 layered cell wall. In the presence of penicillin bacteria lose their rigidity and ability to divide (Landman & Ginoza 1961). In penicillin inhibited staphylococci Park & Strominger (1957) demonstrated the accumulation of mucopeptide constituents in the rigid layer. Cooper (1956) found that radioactive penicillin combines preferentially with the bacillary membrane. Within 10 minutes of penicillin addition the cell begins to leak protein and nucleic acid (Prestedge & Pardee 1957). All this points to the cell membrane as the primary site of action of penicillin.

Streptomycin combines rapidly and reversibly with a surface component of bacteria (McQuillen 1951). Anand & Davis (1960) found increased excretion of nucleotides and amino acids by *E. Coli* in the presence of streptomycin (an altered permeability barrier) indicating an action of streptomycin on membrane formation analogous to that of penicillin on bacterial wall formation. Working with Salmonellae Landman & Burchard (1962) found increased permeability and loss of rigidity concluding that the site of activity of streptomycin is at the bacillary membrane.

Although it might seem presumptuous to assume the same mechanism for action of streptomycin on inner ear sensory cells and bacteria we feel it is a tenable thesis. *The reduction of a rigid wall component and increased permeability of the plasma membrane could explain the changes in shape and swelling of the sensory cells. That the mitochondria are destroyed could be explained by the same type of membrane destructive properties of the streptomycin.* Effects on oxidative enzymes as demonstrated in bacteria by Engelberg & Artman (1961) and Umbreit, Smith & Oginsky (1951) could

as claimed by Landman *et al*, be explained by the fact that these enzymes in most bacteria are connected to the surface membrane

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Dept of Otolaryngology
Karolinska Sjukhuset Stockholm 60 Sweden

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SPLINT STRUTS IN STAPEDECTOMY

A preliminary report

JACOB SADE
Afula, Israel

*From the Department of Otolaryngology (Head J. Sadé M.D.)
Central Emek Hospital Afula*

A modification of the Shea polyethylene prothesis is presented. Its special feature is a sort of bed wherein the long process of the incus lies in a way which prevents sharp pressure on this bone and at the same time, provides stability. It is surmised that this special feature will minimise aseptic necrosis of the incudal long process which is a long term complication encountered in stapedectomies. Early results equal those obtained with other prosthetic forms.

An important part of the discussions at the Second Workshop for Reconstructive Middle Ear Surgery (Chicago March 1963) was devoted to complications arising from the otherwise so very successful stapedectomy operation. The most distressing complication is of course neurosensorial loss whilst a less alarming complication but one causing some concern nevertheless is late necrosis of the lenticular region of the incus.

It seems possible that necrosis of the incudal long process is caused by pressure which in turn is promoted by continuous contact over a long period of time of the prothesis with the incudal long process. Indeed it would seem logical to assume that the firmer the grasp of the prothesis on the long process of the incus and for that matter the sharper the contact between the two the greater are the chances of pressure being conveyed by the prothesis to a limited region of the incus. This situation is met with with the original Shea prothesis (1960) where the incudal tip is in continuous pressure contact with the circumferential polyethylene edge the stable sleeve bearing prothesis described by Goodhill (1961) and possibly also with the so easily introduced Schuknecht wire prothesis (1960). It should be mentioned that we cannot exclude as a cause of lenticular necrosis vascular deficiency of this region following disruption of bloodvessels resulting from removal of the stapes. Anson (1962) has shown that a rich anastomatic circulatory network reaches the incus from the stapes. Alberty in a recent detailed work (1963) shows clearly the multidirectional vascularisation of the incudal long process and the damage that could be caused to it by pressure of a prothesis.

It was with these thoughts in mind that we decided not to discard the vein graft technique until proven wrong, but sought a possibly safer incudo prosthe

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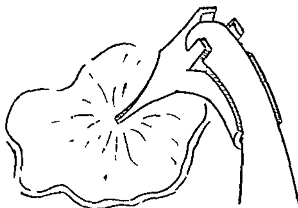


FIG 1

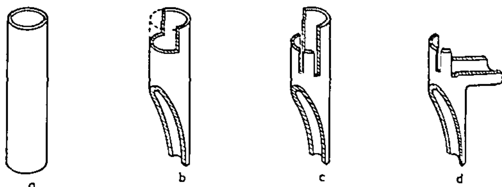


FIG 2

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We used this prothesis so far on a small series ten cases The results are now, after eight months equivalent to those achieved with the other methods, i e with sleeved polyethylene after Goodhill and stainless steel after Schuknecht

RÉSUMÉ

On present une modification de la prothese de polyéthylene de Shea La particularite essentielle de cette méthode est une sorte de massif dans laquelle le long processus de l enclume est placé sans qu il produise une pression aigue sur l os et au meme temps fournit de la stabilité On peut s'attendre que ce facteur reduira la nécrose aseptique du pressus long de l enclume — complication tardive rencontrée dans les stapedectomies Les résultats premiers sont semblables a ceux acheves par les autres formes de prothèse

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Eine Modifikation der Shea Polyethylen Prothese ist beschrieben Ihre Besonderheit besteht aus einer Art von Bett', in welchem der Crus longum incudis liegt Dieses Verfahren vermeidet scharfen Druck auf den Knochen und bietet gleichzeitig Stabilitat Es ist anzunehmen dass dieses Verfahren die aseptische Nekrose des Crus longum incudis — eine Spatkomplikation der Stapedektomien — vermindern wird Fruhergebnisse dieses Verfahrens sind mit denen anderer Prothesen zu vergleichen

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D pt of Otolaryngology Central Emek Hospital
Afula Israel

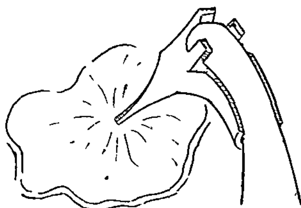


Fig. 1

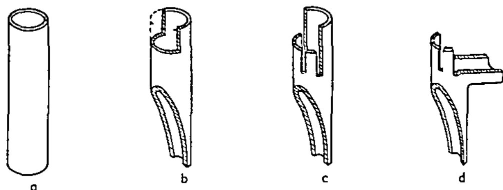


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On présent une modification de la prothèse de polyéthylène de Shea La particularité essentielle de cette méthode est une sorte de massif dans laquelle le long processus de l'enclume est placé, sans qu'il produise une pression aigue sur l'os et au même temps fournit de la stabilite On peut s'attendre que ce facteur réduira la nécrose aseptique du pressus long de l'enclume — complication tardive rencontrée dans les stapedectomies Les résultats premiers sont semblables a ceux acheves par les autres formes de prothèse

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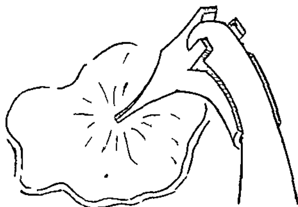


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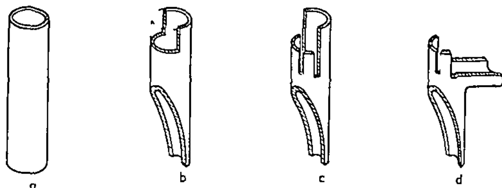


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